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ADDRESSES AND ORIGINAL ARTICLES

TUBERCULOUS DISEASE OF THE ABDOMINAL LYMPHATIC GLANDS

By G. H. Colt, M.B., B.Chir. Camb., F.R.C.S. Eng.
CONSULTING SURGEON TO THE ABERDEEN ROYAL INFIRMARY
AND
G. N. Clark, M.B. Aberd., F.R.C.S. Eng.
ACTING MEDICAL DIRECTOR OF THE ANGLO-SWISS HOSPITAL, ALEXANDRIA

This paper gives the results of an investigation into the symptoms and signs exhibited by patients suffering from the later stages of tuberculous disease of the abdominal lymphatic glands. The patients were admitted into a ward in the Aberdeen Royal Infirmary under the care of one of us (G. H. C.), during the ten-year period 1923 to 1932. The series is a consecutive one of 239 cases, 127 being male and 112 female patients. An effort has been made to trace and examine every patient and has been successful in that 207 have been traced and 118 examined.

Caseous Mesenteric Glands

During the ten years 38 patients with caseous mesenteric glands were operated on, some of them for unrelated conditions, during acute obstruction or for acute appendicitis. Of the 50 cases dealt with by the late Mr. Carson (1918) 44 were of the caseous variety and 6 calcareous. He appeared to be strongly of the opinion that the caseous glands required excision; "The glands which demand operation, therefore, are the caseating glands and those alone." Many surgeons agree with this because of the danger of complications arising when operation is not undertaken.

SYMPTOMS

The duration of symptoms was much less than in the calcareous type, being usually stated either in months or weeks rather than in years. Abdominal pain was always the first symptom. In the majority of patients it was in the right side of the abdomen or in the right iliac fossa. There was usually a history of the pain being generalised across the abdomen, or peri-umbilical initially and later settling in the right iliac fossa, but 5 patients had pain in the left side of the abdomen. There was occasionally a history of radiation across the abdomen to the other side—mostly from right to left; to the back; to the right leg; to the labium (2 cases) and to the shoulder in 1 case. There was apparently no relation between exercise and the pain, only one patient stating that the pain was worse after exercise; 2 patients were relieved on resting. The pain was variously described as "sharp shooting," "stabbing," "like toothache," "severe sharp," "sharp stooning," "spasmodic," "dull ache," "dragging," "steady," and "like a stitch." In one case the pain was sufficiently severe to "double up" the patient. The patients with the longer histories had usually had a series of attacks of short duration with an interval of a month or two between them. The attacks tended to become more severe and were often accompanied by nausea and vomiting. There appeared to be a definite tendency to constipation.

PHYSICAL SIGNS

In all cases except one there was some tenderness in the abdomen situated almost invariably in the right iliac fossa. Hyperæsthesia and increased tonus of the muscles were uncertain and tended to be present only in the cases complicated by appendicular inflammation. A mass was palpable in 8 of the cases. In 3 the mass was in the right iliac fossa; in 2 in the left iliac fossa; in 1 to the right of the umbilicus; and in 1 to the right of the left kidney. Lockwood's sign (Colt, 1932), which is of great value in the diagnosis of adhesions in the cæcal region, was recorded as positive in 4 cases; 3 of these had appendices which were adherent to the cæcum by bands; the fourth had adhesions of the omentum to the peritoneum of the right iliac fossa. Hyperæsthesia over the right lower quadrant was more diffuse and less intense than in appendicitis.

Ketosis.—It was noticed that in the great majority of the subacute and acute cases (both caseous and calcareous) the patient's breath smelt strongly of acetone. In surgical cases this is often due to excessive vomiting with upset of the carbohydrate metabolism. But in the majority of the cases vomiting had been absent or infrequent. When subacute it was often possible to decide by the presence of ketosis that the case, if not one of intestinal obstruction, could be left for medical treatment and operated on later at a safer period. The degree of ketosis in acute appendicular obstruction of equivalent duration is not nearly so pronounced and in fact is often absent.

Pyrexia.—In some of the more extensive and acute cases of caseation and more especially in younger patients the temperature was raised. This was discussed at the Medical Society after Carson's paper. Gauvain supported Carson that there was a rise in temperature in only a few cases, while Warren Low and others were emphatic that the cases they had seen had continued pyrexia. Carson in reply suggested that cases with pyrexia were due to systemic tuberculosis with peritoneal extension. Braithwaite (1925) makes the statement:—

> "It has been suggested that an acutely inflamed gland causes a rise of temperature, whereas acute appendicitis does not. How many men in general practice will agree with this? It is known that almost every painful condition in a child gives rise to an elevation of temperature. A temperature above 100° F. would indicate the condition to be tuberculous adenitis rather than appendicitis."

This is clearly put by John Fraser (1922): "Fever introduces the illness, while in appendicitis temperature is comparatively late in its appearance."

Marshall (1928) in a study of 48 cases of simple ileo-cæcal lymphadenitis finds symptoms very similar to those given here.

Radiological examination was made in 18 of our cases, and in 11 of these, areas of calcification were seen suggestive of glands that had calcified or had begun to calcify. Carson only once observed a vague shadow of a caseating mass by radiography, but he was describing a series of younger patients, in whom calcification in other glands had not taken place. At that time (1918) radiological apparatus and technique were not so efficient as they are to-day. In our series there were a number of caseous cases in which calcified glands were also present. The fuzzy mottled appearance of the latter is typical (see Fig. 3).

None of the writers on the subject of tuberculous mesenteric adenitis appears to have suggested that X ray examination repeated at intervals would be of value in estimating the chances of the patients' recovery. The appearance of well-calcified patches

in a radiogram of the abdomen, where there were none previously, would undoubtedly be a good prognostic sign.

Diagnosis.—Many of these patients were admitted as cases of acute or subacute appendicitis and the figures show that the two conditions frequently coexist. In diagnosing between them the points for and against each may be summarised in the following way. The gland patient may show the several characteristics of either of the two main types that have long been recognised as tuberculous. The sanguine type with her quick intelligence, fine regular features, clear skin, long lashes, and downy hair on the back and arms; and the phlegmatic type with slower intellect, thick skin, and podgy features. In the gland patient there is commonly a characteristic history of previous attacks of pain, which may have been as severe as the present one. In the appendicitis patient the pain is more severe, lasts longer, tends to settle in the right iliac fossa, and is seldom felt on the left side. In the gland patient there may be nausea and possibly vomiting; in appendicitis vomiting is almost certain to occur. In the early gland case the temperature may be raised to 100° F., sometimes more, whereas in appendicitis the temperature will not be raised until several hours have elapsed. In the early stages the pulse-rate will offer little help, but in the late stages it will be greater in appendicitis than in the gland case. The leucocyte count in the early stage of each is low and will not rise appreciably in the gland case, but will soon reach 15,000 to 30,000 in appendicitis. The breath will smell strongly of acetone in the gland case, but not in appendicitis until vomiting has been frequent. If ketosis is present, a general anæsthetic given for making a satisfactory rectal examination would be contra-indicated. The area of hyperæsthesia is more diffuse and less intense in the gland than in the appendicitis patient. This may be due to the situation of the gland—high up in the mesentery compared with the appendix—allowing it to act on nerve-fibres distributed more extensively. Should radiography be possible and positive, and the patient under skilled observation, and should other signs be fairly typical, it would be advisable to adopt the course of clearing the bowel with an enema, giving glucose by the mouth and rectum, waiting a few hours and repeating the leucocyte count. Such a course sometimes allows operation to be undertaken at a less dangerous time or avoided altogether. In case of doubt it will be safer to operate through a right paramedian instead of through one of the smaller incisions.

CLINICAL PATHOLOGY

In reviewing these 38 cases the most striking fact is the large number which had an associated lesion of the appendix. There were 18 cases with some involvement of the appendix—not old signs of inflammation, but active acute inflammation or congestion, in almost half the total number. Either the appendix was giving rise to the symptoms for which the abdomen was opened or the appendix inflammation provided the little extra stimulus for the gland to break down and become caseous. This last explanation should not be taken to mean that all such glands require an added toxæmia from appendicular inflammation to cause caseation. Both explanations seem to have claims to truth and both are probably true. Morley Fletcher (1929a) writing of children describes an "acute localised form" of tuberculous peritonitis. This form, which he calls "appendicular" or "ileo-cæcal," is associated with caseous glands in the ileo-cæcal angle and an injected swollen appendix. He advises removal of the appendix and of the adjacent mass of glands. The appendix was examined microscopically for evidence of tuberculosis in 15 of our cases. In none of them was any evidence of tuberculosis found. Four of the glands removed were examined microscopically and all were tuberculous.

Localised tuberculous peritonitis.—In caseous cases danger arises when small areas of inflamed peritoneum become attached to adjacent coils of gut or to the omentum. When the inflammation subsides, the adhesions may either contract, stretch, or separate completely or the omentum may become stretched out into a tenuous band, which eventually gives way altogether. There have been many instances of this and in one case the gland and its adherent omentum were removed in one piece. On the other hand, when a loop of gut adheres to the mesentery and becomes twisted or kinked or leaves an opening through which another loop of gut can pass, strangulation may occur. The omental band may produce a mechanical obstruction by pressure on the gut. Inflammatory changes in the mesentery itself may shorten it and so bring about conditions favourable to the development of a volvulus or may cause axial rotation of the gut as is referred to under the obstruction series.

Perforation of caseous glands.—Perforation of a gland must be a fairly frequent event. With perforation the risk of acute general tuberculous peritonitis is obviously very great. Widespread bowel and omental adhesions are sometimes instances of recovery from this condition, with subsidence of activity and without persistent ascites. Some cases of acute general tuberculous peritonitis also represent a proportion in which the patient was not able to resist such a sudden infection. In the earlier stages of both varieties there would be free fluid in the abdomen, and the slight rigidity and tenderness associated with it might easily lead to the diagnosis of an attack of mild appendicitis. In this connexion it is interesting to note that Fletcher (1929b) states that *trauma* may have a direct relation to the onset of tuberculous peritonitis. A blow on the abdomen when the muscles were not on guard might easily rupture a caseous gland. There were 2 cases of perforation in our series. In neither was there a history of injury. From what has been said it will be evident that these two cases do not represent the true incidence. Their histories are briefly as follows:

A male, aged 29, with an eight hours' history of generalised abdominal pain coming on immediately after dinner and later settling under the left costal margin. There was a large amount of free fluid in the abdomen and a large perforated tuberculous mesenteric gland with thickened and calcified walls. The gland was incised and drained. The appendix was not removed. He felt in much better health 19 months after operation, and had gained 1½ st. in weight.

A male, aged 20, a farm servant, was admitted after several attacks of abdominal pain during the previous five months. For the last five days the pain had become worse. He vomited on the day of admission. He was flushed, had a dry tongue, foul breath, a temperature of 101·5° F., and a pulse-rate of 104. The abdomen was rigid and slightly tender all over. A large suppurating mass of tuberculous mesenteric glands was found at operation. The mass had perforated filling the abdomen with pus. The appendix was gangrenous. There was generalised miliary tuberculous peritonitis. The perforation in the mass was closed, the abdomen mopped out, the appendix removed, and the abdomen closed. The appendix on section showed miliary tubercles of the serosa, and the pus from the mass and the exudate was

sterile and negative for tubercle bacilli by staining methods. When seen 7 years later the patient was in better health than before, had gained in weight, and had been relieved of his symptoms. He still had frequent pains in the left hypochondriac region which at times almost incapacitated him and were sufficient to cause him to come up to be seen on two occasions with a view to further operative treatment.

It seems that the first patient overcame the tuberculous process completely and the second now suffers occasionally from the effects of intra-abdominal adhesions.

TREATMENT

Surgery.—In 29 of the 38 cases (more than three-quarters) it was possible to excise the affected glands. This does not mean that all the calcareous and enlarged glands were resected in any one patient; usually all the larger and caseous glands were excised and any calcareous glands which were considered likely to give rise to trouble in the future. When it was not possible to excise the glands completely, either on account of the bad condition of the patient, or from the position in the mesentery, or on account of the size of the mass with its surrounding induration and œdema, evacuation with a spoon or scoop was resorted to after an incision had been made into the capsule. There were 5 such cases; a sixth might be added where the procedure was to incise the mass, swab it out and leave in a drain, because secondary infection was suspected. Evacuating the contents of the gland capsule does not appear to be the ideal procedure, but it is often the only one compatible with safety.

Sinus formation is commented on by Braithwaite and he advises against the removal of a gland near the mesenteric border in case a fæcal fistula results. In a good coloured picture of such a case, the segment of gut near the gland is shown inflamed and somewhat contracted. He recommends isolation by omental graft when removal is difficult.

Therapeutics.—It has been suggested in the past that attempts might be made to hasten calcification by giving calcium salts. More recent work on the calcification of tubercles in experimental animals shows that irradiated ergosterol or vitamin D has a great effect in the promotion of calcification of caseous tubercles in rabbits (Levaditi and Li, 1931) and guinea-pigs (Jampolis and Witt, 1933). The beneficial effect of sunlight both natural and artificial in the general treatment of the disease may be largely due to this process of calcification sealing up the tuberculous areas. It may well be that the degree of calcification in the other areas of the body liable to tuberculosis and the benefit likely to ensue from ultra-violet radiation are very closely related—e.g., calcification in the lung lesions is relatively rare, and ultra-violet radiation is understood to be contra-indicated in phthisis. Jampolis and Witt are cautious in so far as they point out the fact that the conditions in the animals experimented on are not directly applicable to man. A warning may be noted here in the treatment of caseous patients by ultra-violet light or sunlight. Carson (1926) quoted Rollier in an excellent article on tuberculous peritonitis to the effect that sun treatment produces its best results in the ascitic type, but in the caseous type a congestive reaction accompanied by vomiting and fever may occur. Vitamin D increases the serum calcium and phosphorus and both are then retained in greater quantities in the body. Milk is the most important food containing calcium. Absorption of calcium is promoted by an alkaline digestive juice. Practically, therefore, the patient should be given vitamin D, exposed to ultra-violet rays, and encouraged to drink milk with some sodium bicarbonate some time before meals. The mineral salts are supplemented, if need be, by the administration of calcium and phosphorus. As in cervical tuberculosis it will be obvious to anyone who has had a long experience that there is much uncertainty in any method of palliative treatment. In some cases a diagnosis is not possible in the abdominal cases until the abdomen is opened. Radical treatment at the time is then more appropriate. Glands which are merely swollen should not be removed. A piece may be taken for biopsy and the abdomen closed.

TABLE I

Results of Treatment

Traced.	Untraced.	Excellent.	Fair.	Poor.	Died.
36	2	27	3	1	5

It seems also that, when a preoperative diagnosis of caseous glands has been made, the safest treatment is removal. Such patients are liable to develop grave complications at any time if nothing radical is done. One should, however, avoid operation if repeated radiological examination shows that calcification is actively progressing. From the suggested relationship between a diseased appendix and caseation it seems that the appendix should generally be removed.

The results of treatment in the 38 cases are shown in Table I.

Calcareous Mesenteric Glands

This part of the paper is based on a study of 201 consecutive cases summarised in Table II.

TABLE II

Summary of Cases with Calcareous Glands

Nature of case.	Traced.	Untraced.	Males.	Females.	Total.
Calcareous cases ..	144	22	91	75	166
Reoperation cases	31	4	15	20	35
—	175	26	106	95	201

It has been assumed that the calcareous glands were at one time caseous and have run their usual pathological course. In the absence of any definite information we may take it that the majority of glands are well on the way to complete calcification at the end of a year after they have been infected with tubercle; many have probably commenced to calcify within half that time. Radiological evidence in a series of patients of different ages would be most valuable if it could be obtained.

The dangerous period.—During a period then of a few months to a year or more, each caseous and calcifying gland may be a source of danger. This does not necessarily correspond with the period during which the patient is actually in danger. One or two glands may caseate and commence to calcify. Others may break down some considerable time after the first. The cycle is gone through again with another danger period to the patient. There is no doubt about this happening as in some of the cases caseous glands coexisted with calcified glands. Clinically this repeated cycle was recognised by Hutchison (1925) when he wrote:—

"I do not think one has a right to say that a case is completely cured simply because after a few months the

symptoms have not recurred. The disease is apt to remain latent for a considerable time. Such a child may, perhaps, get an attack of diarrhœa, or other slight illness, which pulls him down, and, his resistance for the time being lowered, the process flares up again."

The sequence would be an intestinal upset, increase in caseation with more rarely the bursting of a caseous gland, and the onset of a more or less localised tuberculous peritonitis. The second attack would tend to be of slighter extent because of the adhesions left by the first, and of less severity on account of the resistance developed by the patient.

Effects of natural cure.—That a natural cure by complete calcification occurs in a very large percentage of cases must be obvious. In many cases the cure is complete from the patient's point of view—he has no symptoms whatever. The glands are in a position in which they are not liable to press on any of the important intra-abdominal structures. They are of such a size and shape that they do not rub on adjacent structures when strenuous movement causes the abdominal contents to change their positions. A possible or, judging by operation cases, a probable exception is when there is a spike of calcareous matter sticking out of the gland, or when the surface is crenated as is often observed. Even small masses of this kind give rise to symptoms. It seems therefore that obese subjects would be less liable to suffer than the thin, since the glands would be surrounded by fatty beds which would tend to distribute their pressure more evenly over a larger area. These calcareous masses must have very little tendency to contract; once calcified, their shape and size tend to remain the same, a fact very much in the patient's favour, or had healing taken place by fibrosis there would be a continued contraction of the area with a greater liability to the narrowing of the blood-vessels, to the obliteration of lymphatics, to pressure on nerves, and to distortion and shortening of the mesentery. If a large number of the glands were destroyed, the passage for the fat might be inadequate.

Effect on fat absorption.—That tuberculous disease of the mesenteric glands does embarrass the absorption of fat is undoubted. Still (1927) gives a good illustration from a specimen which showed the engorgement of the lacteals with caseous material and "perhaps also some fat." The lacteals are seen to be connected with an enlarged gland in the mesentery. Only a few of the lacteals are affected. If the diseased glands were very numerous and situated near or actually at the root of the mesentery there would be considerable interference with the absorption. Talbot (1912) has shown that fat absorption may be prevented by the enlarged glands blocking the lymphatics. In our own series there was no gross evidence of serious non-absorption of fat apart from the fact that some of the patients on admission were described as being thin or poorly covered. Again after operation when it might be expected that the additional fibrosis would constrict the lacteals even more, there was no case with excessive wasting in those examined. The operative relief of pressure on the vessels had been adequate.

Unusual end-results.—The development of calcification is not limited to the glands themselves. Tubercles on the peritoneal surfaces may become calcified as was found in one of the cases. The most likely explanation of this is that they have resulted from healing in an area of generalised tuberculous peritonitis that has become caseous during the acute stage.

A female, aged 28, had had an operation 5 years before for a psoas abscess. She had passed pus by the bowel 3 years previously. She was found at operation to have bilateral tuberculous salpingitis, an irregular calcareous mass at the root of the mesentery, an omentum showing many apertures, and in addition *numerous calcareous tuberculous nodules studded all over the abdominal peritoneum.* There were also numerous omental bands which were not giving rise to obstruction. This patient was untraced after operation.

It is interesting in this case to note that there was an appendix abscess, which was thought not to be tuberculous, and also the presence of the omental apertures, which may have been caused by the breaking away of the omentum from the caseous areas when they had become calcified.

SYMPTOMS AND SIGNS

In a large number of cases, calcareous glands are present in the abdomen without giving rise to any complaint whatever. They are discovered by accident in radiological examination for some unrelated condition such as a fracture of the pelvis. Such a case is exemplified in Fig. 1, taken from a male patient suffering from hæmorrhoids, who had lived to the age of 65 years without having a single abdominal symptom. The main symptom that may be ascribed to the presence of calcareous mesenteric glands is generalised abdominal pain later settling in the right lower quadrant of the abdomen. It is dragging or colicky, and sometimes radiates to the thigh and back and is accompanied by nausea and occasionally by vomiting. In many of the cases the pain is liable to come on in repeated attacks of relatively short duration and is especially worse after exercise and when the patient is fatigued. There is usually a tendency to constipation which is worse during the attacks. There may be some degree of relationship between the menstrual cycle and the occurrence of the pain. Frequently the pain commences in the left abdomen and radiates to the right. Some of the patients complain of discomfort some hours after food, some immediately after. Backache is also commonly complained of. Auchincloss (1930) lays stress on night discomfort after a hard day's exercise and thinks it is due to venous congestion by pressure of the node. Aggravation of the symptoms by work or exercise has been very frequently noted in our series of cases. When this is so, rest usually brings relief. Often from the history alone a mistaken diagnosis of duodenal ulcer has been made.

PHYSICAL SIGNS

Apart from some slight tenderness and hyperæsthesia in the right lower quadrant of the abdomen or the umbilical region, there may be no other physical sign to be made out. There may be some rigidity in the right iliac fossa. Infrequently a palpable mass may be felt in some part of the abdomen. In this series there was a mass palpable in 11 cases, but of these probably only 5 were due to enlarged glands. The situation in all 5 was in the right iliac fossa and one of the masses was tender. In another case an indefinite mass was felt in the epigastrium, but it is doubtful whether it was glandular. There is usually some distension of the abdomen which may be more marked during attacks of pain. Lockwood's sign was present in 33 cases. In 29 of them the appendix was found to be bound down to the cæcum by adhesions. The constancy of the sign makes it very valuable in the diagnosis of chronic appendicitis. An opportunity occurred of testing Lockwood's explanation of the mechanism of its production.

A patient was admitted suffering from pain, nausea, and vomiting of eight days' duration. The diagnosis was

one of chronic appendicitis. The sign was positive. At the operation the appendix lay with its tip anchored over the pelvic brim, and the lower end of the ileocæcal valve was on the stretch. On pressing the cæcum, before the appendix was removed, fine crepitant gurgling occurred, and could be repeated as often as desired. After removal of the appendix and freeing of the tension, the sign could no longer be elicited.

Golden and Reeves (1929) point out that the leucocyte count is not raised in calcareous gland cases and this would seem a valuable aid in the differential diagnosis from acute and subacute appendicitis.

The *radiological examination* of the abdomen is generally conclusive, but it is not uncommon for the reports on gland cases to be misleading. This is often due to the gland overlying the lumbar spine or the iliac bones. If examined carefully and with the eyes on the look-out for the glands they can be easily seen in the film even if they overlie the bodies of the vertebræ (Fig. 2). Out of the 201 cases, 110 were subjected to X ray examination of the abdomen. Of these, 84 were reported to have calcareous glands present. Thus 26, almost a quarter of the total number examined, were missed on ordinary examination of the films, but some of these may have been only caseous. The glands are generally seen round a line extending from the left side of the 2nd lumbar vertebra to the right sacro-iliac joint—i.e., in the line of attachment of the mesentery. They are of irregular shape and have fuzzy outlines. The larger ones are speckled, being apparently composed of many centres of calcification. The typical appearance resembles no other pathological condition (see Fig. 3). In our experience ketosis is common. The odour of acetone in the breath or its detection in a sugar-free urine should lead to a radiological examination of the abdomen.

The conditions which might be confused are phleboliths, ureteric stones, enteroliths, and opaque bodies in the bowel, stones in a low-lying kidney or gall-bladder and calcareous deposits in an infected kidney. In any case of doubt, stereoscopic pictures will often settle the matter or the methods usual in pyelography will help. A good illustration of this is the following:—

A married woman of 29 was sent for consultation on account of a feeling of heaviness and discomfort in the upper abdomen after meals and dating from pregnancy 3 years previously. The patient had had occasional difficulty in urination but no frequency. The urine was found to be normal. X ray examination showed a small calcified gland in the right upper abdominal quadrant but no gall-stone. Visualisation of the renal region and of the gall-bladder shows its relationship to these organs. The latter film shows a small lighter area in the lower third of the gall-bladder which is probably a single cholesterin gall-stone. The patient's symptoms scarcely warranted operation and she was discharged. Unfortunately she left the district and has not been traced.

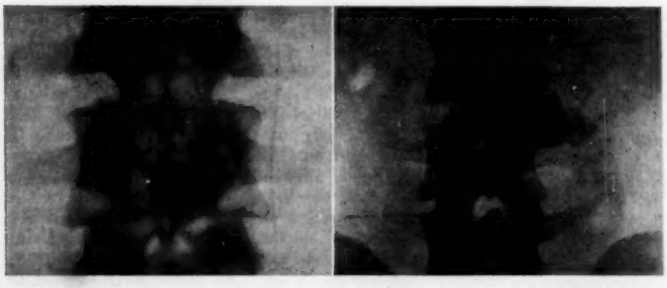

FIG. 2.—Radiograms of a case with calcified mesenteric glands; on the left, hidden by the shadow of the middle vertebra; and on the right, revealed by displacement of the mesentery.

RESULTS

Of the 166 cases that required operation, 22 were untraced. More than half of those traced were examined and the remainder received a questionnaire.

FIG. 1.—Calcified glands in the right iliac fossa; from a man aged 65 who had no symptoms.

Of the 201 cases, 35 required reoperation; 3 patients died shortly after operation, 2 of them having been admitted with acute obstruction, and the third being in a very obese female whose wound burst 9 days after the removal of a chronically inflamed appendix and a few calcareous glands and the freeing of some light adhesions. Recent general peritonitis was present, the cause of which was not apparent at the post-mortem. The fourth death occurred suddenly two years after post-operative hemiplegia from mitral stenosis. The remaining 163 cases are classed in five groups:—

Group I had 19 cases, discovered at operation performed for conditions in the abdomen other than appendicular disease and bands, and included here for the sake of completeness. We have called them "accessory cases." Briefly, there were 6 with duodenal ulceration, 2 with gall-bladder disease, 5 had retroversion of the uterus which was treated by operation in 2 cases; 1 had a perforation of the gut by a fish bone, and another had a testicular tumour removed; 3 had ovarian cysts, 1 of which was very large; 1 was complicated by bilateral tuberculous salpingitis; in all 17 were traced, 9 being excellent results, 3 good, and 2 poor. One case of carcinoma of the appendix showed a good result three years later. There were 3 deaths.

Group II.—A few cases in which glands were seen at operation but were not removed.

Group III.—Those in which the appendix was found to be subacutely or acutely inflamed, ulcerated, or injected.

Group IV.—The largest of all the groups includes those cases where the appendix was found either to be

chronically inflamed or of the atrophic variety, and one case of doubtful tuberculosis of the appendix. There was one death.

Group V.—Where the condition of the appendix was not stated and assumed by us to be normal, or where it was found to be normal.

The accompanying Table III summarises the results.

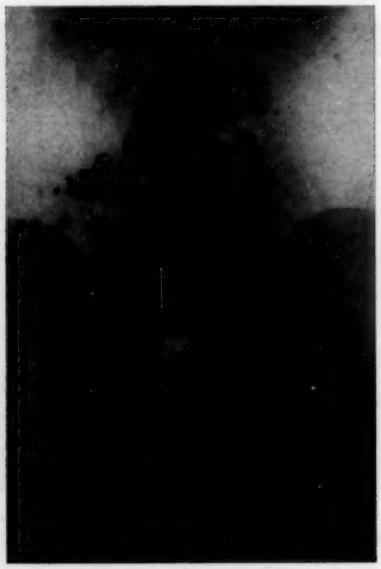

FIG. 3.—Multiple calcification, showing appearance and distribution of the shadows.

Reoperation Cases

Of the 201 patients (excluding the 38 caseous cases) who were operated on 35 required more than one operation on the abdomen. There were 15 males (of the total 106) and 20 females (of the total 95). Two operations were needed in 21 cases, 11 had three operations, 2 had four operations, and 1 had five operations. We traced 31 of these cases; 1 patient had died and 4 remained untraced. In their results, 16 were good and 14 unsatisfactory.

No surgeon seeks these operations, they are done only from necessity and when the symptoms are considered to be due to a lesion that can be rectified without producing a worse one. In the interval, all ordinary care in diet is exercised by the patients and the use of aperients forbidden. A filling diet and slow-circling exercises three times a day has often given excellent results in those suffering from what might be called "aperient-itis." This is certainly true before the first operation in chronic cases.

Prophylaxis.—It is even more difficult to generalise from these cases than in the cases of calcareous glands. Since September, 1929, saline has been left in the abdominal cavity in most cases which were not acute. Usually two pints but sometimes more were used, the maximum being five pints. It is difficult to give any figures to support the impression, but it seems that the results after the use of saline had been adopted were much better than before. Apart altogether from the improvement in the patient's outlook from the prevention of adhesions, there was a very pronounced and almost immediate improvement in the condition of the pulse on the introduction of the fluid.

In considering reoperation on adhesion patients it is essential, unless acute symptoms develop, to allow time for the abdominal contents to settle down after the trauma of the last operation. The ward sister states that the immediate post-operative condition is always more troublesome in these cases than in many so-called larger operations. Even in patients who had only one operation, we were struck by the numbers who had a fair amount of abdominal discomfort up to six months after operation and even longer. In many cases adhesions disappear altogether if left for a long time. If the patient's life is a misery at the end of two years operation should be undertaken.

Tuberculosis of the Appendix

During the period under consideration 106 appendices were submitted to microscopical examination for evidence of tuberculosis. Of these, 93 were from cases of caseous and calcareous mesenteric glands and the other 13 were included because of some irregular thickening or sclerosis observed at operation; 3 only showed evidence of tuberculous disease. In 1 of the 93 gland cases a single minute area alone showed signs of actual tubercle, but 8 showed prominent and active lymphoid deposits in the mucosa.

Among the 13 cases included—no diseased glands being present—because of irregular thickening or sclerosis, were 2 of undoubted tuberculosis. In both cases the disease was limited to the appendix itself and *in both the mesenteric glands were unaffected*, which shows that the statement made by Sir William Willcox (1934) may not always hold: "I would remind you that one sometimes meets with a tubercular appendix. That may possibly be diagnosed by the history of the case, but at operation it is diagnosed by the presence of tubercular glands."

TABLE III

Operative Results

Group.	Traced.	Untraced.	Excellent.	Good.	Poor.	Bad.	Died.	Total.
I Accessory cases ..	17	2	9	3	1	1	3	19
II Glands not removed ..	6	0	3	1	1	1	0	6
III With acute or subacute appendicitis	36	6	32	1	1	2	0	42
IV With chronic appendicitis	71	13	56	9	2	3	1	84
V With normal appendix	14	1	9	3	1	1	0	15
Totals	144	22	109	17	6	8	4	166

Conclusions

(1) The caseous stage of tuberculous mesenteric glands is the dangerous one from the point of view of the spread of the disease, the complications, and the mortality. (2) Bursting of a caseous mesenteric gland is probably a fairly frequent event and results in various degrees of tuberculous peritonitis. (3) Caseous mesenteric glands are a common cause of pathological conditions leading to intestinal obstruction. (4) There is apparently a relationship between the caseation and the inflammatory conditions of the appendix. Caseous glands should be removed when found at operation and appendicectomy carried out as a routine. (5) Adhesions and bands of various kinds often result from the healing of subacute tuberculous peritonitis. (6) Calcareous mesenteric glands alone frequently give rise to symptoms and

require to be removed. (7) Appendicectomy alone is sometimes done in acute or subacute cases when tuberculous glands are the cause of the symptoms. (8) Abdominal tuberculosis in young adults, according to other workers, appears to be more severe than that found in a ward for general surgical cases. (9) There appears to be very little liability to the "stirring up" of a tuberculous lesion when glands are removed even if they are caseous. (10) The administration of intraperitoneal saline at the end of the operation tends to prevent adhesions. (11) Reoperation should not be undertaken, if it can be avoided, before two years have elapsed. (12) Progressive calcification in mesenteric glands, as shown by repeated X ray examination, can be a guide in prognosis. (13) Tuberculosis of the mesenteric glands tends in the main to natural cure.

We are indebted to the honorary staff of the electrical department of the Aberdeen Royal Infirmary for the loan of many radiograms; to the late Dr. G. M. Duncan for the examination of the pathological material and for his advice on numerous occasions; to Dr. G. S. Banks for his reports on the patients admitted to the Municipal Hospital; to Prof. Shennan and his assistants in the pathological department of the University of Aberdeen for the reports of the post-mortem examinations; and to the ward sister and the members of the nursing staff of the Aberdeen Royal Infirmary for their help on many occasions.

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INTRADERMAL TESTS FOR SUSCEPTIBILITY TO WHOOPING-COUGH

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IN the sphere of communicable disease, the prevention and control of whooping-cough is now regarded as one of the most serious problems confronting public health authorities. The disease is responsible for 2000–3000 deaths annually in England and Wales, and as many as 40,000 cases of the disease are said to occur every year in London alone. These figures do not reflect the vast amount of physical and nervous suffering, the loss of school attendance, and the risk of impaired health and lowered resistance to tuberculosis that those who survive an attack of whooping-cough are apt to incur.

It must be admitted that in the past efforts to control this disease—by school notification, isolation of sufferers, exclusion of contacts and, more recently, administration of convalescent serum—have not been attended by any substantial measure of success. Within the last few years, however, the suggestion that methods of specific immunisation might be effectively employed in whooping-cough prophylaxis has brought renewed hope, and in spite of recent efforts to implicate filtrable viruses in the causation of the disease, Sauer's claim that he can immunise children against pertussis by means of a specially prepared vaccine of the Bordet-Gengou bacillus continues to command serious attention.

THE TEST

A little more than a year ago Paterson, Bailey, and Waller (1935), while confirming in the main Sauer's results, attempted to devise a skin test of susceptibility to whooping-cough, using as their antigen Sauer's vaccine. The present investigation, prompted by this latter work, is an effort to estimate the reliability of this intradermal test as an index of susceptibility. So far I have made no attempt to assess the practicability of active immunisation by Sauer's technique.

The test is based on the skin reaction to an intradermal injection of Sauer's vaccine (1933) which is made from 5–7 strongly hæmolytic strains of *Hæmophilus pertussis* (*B. pertussis* of Bordet and Gengou) isolated from early cases of whooping-cough by the cough-plate method.

The bacilli are grown for 48 hours in an incubator on the cherry-red Bordet medium made with freshly defibrinated human (placental) blood. The bacilli are scraped off and suspended in 0·5 per cent. phenolised physiological salt solution and left to stand in a refrigerator for one week. Sterility is ensured by culture on three successive days. The concentrated vaccine is then diluted until 1 c.cm. contains approximately ten billion bacilli and it is stored in a refrigerator until required for use.

Technique.—Into the forearm 0·1 c.cm. of Sauer's vaccine is injected intradermally so as to produce a raised weal. The skin reaction at first was read at 24 and 48 hours after injection, but subsequently the 48-hour reading was discontinued as it was found that strongly positive reactions at 24 hours had very often so faded as to make an accurate reading impossible at 48 hours. Careful observation showed that in all cases where a positive skin reaction developed it did so within 12 hours of injection. It was further noticed that strongly positive reactions at 12 hours were often much less definite 12 hours later. In the latter half of this investigation accordingly the reactions were read at 12 hours and again at 24 hours after injection.

Reaction.—A positive reaction varied widely from a mild hyperæmia of the skin at the site of injection, circular in form and about 10 mm. in diameter to an intense hyperæmia at least 30 × 20 mm. in extent with raised edges and some induration. This latter type of reaction faded from red through pink to brown and had usually disappeared in 72 hours without leaving any residual staining.

At first the interpretation of the milder reactions gave rise to considerable difficulty, and until 100 cases had been tested there was a tendency to regard as positive reactions which with further experience one learned to classify as merely the response of the skin to the trauma of the needle. In particular with the sensitive skins of infants up to 18 months of age, this traumatic factor was apt to show itself and resulted in a certain number of reactions being interpreted as positive in cases where there was no doubt about the absence of any history of whooping-cough. This possible fallacy (referred to again later) must be borne in mind in considering the results of the present investigation. Although the difficulty of interpretation would appear to lessen the value of the test for routine diagnostic purposes it should be made clear that with further experience it was

found possible to differentiate between purely traumatic responses and the true positive reaction in every case.

A positive reaction is here taken as connoting immunity to pertussis, although it is realised that objections might be raised to this on the ground that the skin reaction would be given by persons who were sensitive to other members of the group—e.g., *Hæmophilus influenzæ*—while non-immune to the Bordet-Gengou bacillus. Again, it might be urged, on the analogy of the Mantoux test in relation to tuberculosis, that a positive skin reaction indicated merely previous experience of the bacterial antigen short of immunity to clinical pertussis. But, it is submitted that the antigen used in this investigation—viz., a specially prepared vaccine containing the whole Bordet-Gengou bacillus—places the test on a different plane to the Mantoux, to group intradermal tests, and to the test recently described by Siebler and Okrent (1934).

RESULTS

The test was originally performed on children and adults irrespective of age but was subsequently restricted to children under 10 years of age owing to the difficulty of obtaining a reliable history of previous infection in adults. This difficulty existed also to a less extent in children, but the history of previous infection can be personally vouched for in all cases included in the present investigation. The Table gives the results of the investigation. The

Results of Skin Test for Whooping-cough (371 *Cases*)

Past history.	Reactions.			
	Positive.		Negative.	
No whooping-cough ..	40	29%	208	90%
Whooping-cough ..	99	71%	24	10%
Total	139	100%	232	100%

fact that 40 cases gave immune reactions in spite of no history of clinical whooping-cough is at first sight rather disconcerting, but when allowance is made for the development of immunity in a highly urbanised population because of repeated small doses of *H. pertussis* causing subclinical varieties of the disease, this discrepancy becomes more understandable. Latent epidemics must be fairly active in a city with housing conditions like Dublin. Furthermore it is generally agreed that not more than 60 per cent. of all children in a community exhibit frank manifestations of whooping-cough at some time or other (Leslie and Gardner 1931). While the escape of the remaining 40 per cent. may be due to absence of exposure to infection, an inherent resistance to disease is admitted by all epidemiologists. An instance of this noticed in the present investigation was in the case of two brothers A and B, aged 4 and 6, who both showed strongly immune reactions although only A had suffered from whooping-cough.

During the investigation certain interesting features emerged.

(1) Four cases of whooping-cough seen late in the spasmodic stage all showed strongly immune reactions.

(2) A case of scarlet fever who had been in contact with whooping-cough was found on routine testing to show a non-immune reaction. In due course he developed whooping-cough, and five weeks after the first test was retested when he gave an immune reaction.

(3) There were 9 cases in close contact with a case of whooping-cough but with immune reactions, who never developed the disease although only 2 of these had a definite history of a former attack.

(4) A child suspected of developing whooping-cough gave a negative (non-immune) reaction. Under observation the suspicion was dismissed on clinical grounds. Repeated tests with Sauer's vaccine gave a persistently negative (non-immune) response.

(5) Although active immunisation was not included in the scope of this preliminary investigation three children with non-immune reactions were given a course of immunising injections with Sauer's vaccine, receiving three weekly subcutaneous doses of 1 c.cm., 1·5 c.cm., and 1·5 c.cm. into each arm, making a total of 8 c.cm. for each case. Tested one week after the third injection all had strongly immune reactions.

CONCLUSIONS

A series of 371 cases were examined for susceptibility to whooping-cough by an intradermal test, using Sauer's vaccine as an antigen: the results were compared with the history of previous infection.

The results of skin testing show a high measure of correlation in those patients having non-immune reactions, 90 per cent. of whom gave no previous history of whooping-cough.

A slighter measure of agreement between the result of the test and the previous history was shown in the case of those giving immune reactions, 71 per cent. of whom were known to have had an attack of whooping-cough. It is certain that some at least of these reactions were incorrectly read as positive (or immune) at the commencement of the investigation.

Certain incidents—the insusceptibility of positively reacting (immune) patients after exposure to infection, and the change of the reaction from negative to positive after an attack of whooping-cough—support the view that the test is, within limits, a reliable index of susceptibility to *H. pertussis* infection.

I wish to express my thanks to Dr. C. J. McSweeney, medical superintendent of the Cork-street Hospital, at whose suggestion this work was undertaken, for help and encouragement during the investigation.

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THE DIAGNOSIS OF WHOOPING-COUGH

THE COMPLEMENT-FIXATION AND INTRADERMAL TESTS

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The landmarks in the laboratory diagnosis of whooping-cough are briefly the following:—

In 1906 *Bacillus pertussis* was first described by Bordet and Gengou as the causal organism of whooping-cough. They also found (1907) that the serum of patients convalescing from whooping-cough had the property of deviating complement when *B. pertussis* was used as antigen. Leucocytosis in whooping-cough had been previously described by Frölich (1897), while later investigators found that a relative lymphocytosis was the outstanding feature in the hæmatological picture. The bacteriological diagnosis of whooping-cough by the "cough plate method" was introduced by Chievitz and Meyer (1916), and has since been used extensively in Denmark and other countries with considerable success

in the early diagnosis of the infection. In 1931 Leslie and Gardner, dealing with the antigenic structure of the organism, clarified the confusion on the subject by describing four antigenic phases of *B. pertussis*, Phase I being the most toxic and the best antigen for vaccines; with Phase II it corresponded with the "smooth" state, Phases III and IV with the "rough" state of other organisms.

An intradermal test for the diagnosis of whooping-cough has been used by several investigators with varying results. Siebler and Okrent (1934) came to the conclusion that children with a previous history of whooping-cough usually gave negative skin tests, the converse being also true—that children with no previous history of whooping-cough usually gave a positive skin reaction. The vaccine used by these investigators was one prepared in a similar manner to that used by Sauer (1933). On the other hand, Paterson, Bailey, and Waller (1935), also using Sauer's vaccine, found that children with a previous history of whooping-cough usually gave a positive skin reaction, whilst children with no previous history of whooping-cough gave a negative skin reaction. In a subsequent letter in the same year, Paterson (1935) stated that the results obtained varied with the batch of vaccine used.

Methods and Material

The material used in the present investigation consisted of patients suffering from whooping-cough with or without complications, who had been admitted to the wards of Belvidere Hospital during the epidemic of whooping-cough in Glasgow in the winter of 1934–35; children convalescing from broncho-pneumonia during the following winter were used as controls.

TECHNIQUE OF THE COMPLEMENT-FIXATION TEST

The antigen used in the majority of the complement-fixation tests was the St. Mary's Hospital prophylactic A vaccine issued by Parke, Davis and Co. in a concentration of 4000 million whole *B. pertussis* per c.cm. This vaccine is stated to be prepared from smooth strains of *B. pertussis*. It was found that a dilution of 1 : 5 of this antigen had practically no anticomplementary effect.

TABLE I—*Complement-fixation Tests*

M.H.D. of complement.	2	3	5	Serum control 2	Result.
Hæmolysis	c.	c.	c.	c.	Negative.
"	m.tr.	c.	c.	c.	Doubtful positive.
"	tr.	a.c.	c.	c.	Weak positive.
"	0	tr.	c.	c.	Positive.
"	0	0	c.	c.	Positive.

M.H.D. = minimum hæmolytic dose. 0 = no hæmolysis; tr. = trace of hæmolysis; m.tr. = marked trace; a.c. = almost complete hæmolysis; c. = complete hæmolysis.

In the test proper 0·25 c.cm. of the diluted antigen was added to each of 4 test-tubes. To each of these, and to a fifth serum control tube containing 0·25 c.cm. of normal saline, the patient's serum was added in amounts which varied from 0·05 c.cm. in the first series of cases to 0·2 c.cm. of serum from the later batches of sera, this latter amount of sera having been considered to be the optimum amount of serum for the test. The complement dose of fresh guinea-pig's serum was estimated for 0·5 c.cm. of sensitised sheep cells (3 per cent.) and 2, 3, 5, and 7 doses of complement were added to tubes 1, 2, 3, and 4 and two doses to the fifth serum control tube. In the later complement-fixation tests the fourth test-tube, containing 7 doses of complement, was omitted. The test-tubes and their contents were incubated for 1½ hours at 37° C., after which 0·25 c.cm. of sensitised sheep cells (3 per cent.) was added, incubation being carried out for a further hour at 37° C. In each batch of complement-fixation tests, serum and antigen controls were put up, and a positive human or rabbit serum was included in the tests.

Table I indicates how the readings were recorded. In the analysis of results "doubtful positive" reactions were recorded as negative.

In order to test the antigenic efficacy of the various vaccines a rabbit was given intravenous injections of the St. Mary's vaccine and complement-fixation tests were done in the usual way, using St. Mary's vaccine, Madsen's Danish vaccine, and Sauer's vaccine. All the vaccines fixed complement satisfactorily, best results being given with the Sauer vaccine.

TECHNIQUE OF THE INTRADERMAL TEST

The following vaccines were used for the skin test:

(1) Sauer's pertussis vaccine containing 10,000 million organisms per c.cm.

(2) Whooping-cough dissolved vaccine containing the dissolved constituents of 4000 million or 8000 million organisms per c.cm., prepared by the Glaxo Laboratories Ltd.

(3) Whooping-cough vaccine (prophylactic A) containing 4000 million organisms per c.cm., prepared by the Inoculation Department, St. Mary's Hospital (issued by Parke, Davis and Co.).

(4) Kreuger's bacterial antigen prepared by mechanical disruption of masses of *B. pertussis*, 1 c.cm. of the undenatured antigen being roughly equivalent to 10 billion bacilli.

All of these vaccines consist of whooping-cough bacilli alone, either in the intact state (e.g., Sauer's and St. Mary's vaccine), mechanically disrupted (e.g., Kreuger's vaccine), or chemically dissolved (e.g., Glaxo vaccine). None of the vaccines used were in a dilution lower than 4000 million organisms per c.cm.

In each case 0·1 c.cm. of the vaccine was injected intradermally on the flexor aspect of the forearm, the proper antigen control being used for each different type of vaccine, except in one case where Kreuger's vaccine was used without a control. The readings were taken when the reactions were at their height, usually 18 hours after the test had been done. Later readings were also taken, but these were invariably found to be less intense than the 18-hour readings.

A skin reaction was considered positive when the area of redness was 1 cm. or more in its longest diameter, the control test being negative. There is usually an area of induration which may or may not be more than 1 cm. across in each skin test if it is positive: this indurated area when present is both visible and palpable.

Results

THE COMPLEMENT-FIXATION TEST

The results of the complement-fixation tests will be considered in two groups: (1) cases not treated therapeutically with *B. pertussis* vaccine, and (2) cases so treated. In each of these groups a special analysis will be made of cases with negative reactions, in an attempt to find out the causes of the negative tests. There is a third group of control cases.

Group 1: *non-vaccine treated.*—There were 58 patients in this group, of whom 44, or 75·8 per cent. gave positive complement-fixation tests.

The average duration of infection from the onset of the illness until the blood had been withdrawn was 42·54 days. Patients from whom blood had been withdrawn on or before the twenty-first day of illness numbered 21, of whom 15, or 71·42 per cent., gave positive complement-fixation reactions. The duration of illness from the onset until blood was withdrawn in the remaining 6 cases

with negative complement-fixation tests was respectively 6, 9, 10, 18, 19, and 21 days. There were 37 patients who had blood taken off after the third week of illness, and of these 29, or 78·40 per cent., gave positive complement-fixation tests. An analysis of the reactions according to age-groups in these 58 cases suggests that the antibody response is less active in the younger children, so that negative tests are most likely to occur in the younger age-groups (see Table II).

TABLE II—*Variation with Age*

Age in years.	Number of cases.	Negative.	
		Number.	Per cent.
0–2	15	5	33·3
2–5	34	9	26·4
5 and over ..	9	0	0

When the 14 cases with the negative complement-fixation reactions were further analysed various factors possibly responsible for a negative reaction were elicited. These are as follows:—

1. Extreme youth: 4 cases were less than a year old when blood was withdrawn.
2. A short duration of illness before the blood was withdrawn: 6 cases had blood withdrawn 3 weeks or less from the onset of the disease.
3. Anticomplementary sera: 3 cases were labelled as having negative complement-fixation tests because their sera were anticomplementary.
4. A severe form of whooping-cough: 2 cases had severe whooping-cough when the blood was withdrawn.
5. The presence of acute complications: 2 cases had broncho-pneumonia when blood was withdrawn.
6. In addition, in 6 cases, less than what was later regarded as the optimal amounts of antigen or serum or both was used, while 6 of the 14 cases were recorded as "doubtful positives."

It may be noted that in the above analysis of the various factors tending to produce a negative result each case may have been influenced by one or more factors. It is of interest to note that in two cases the complement-fixation tests which were at first negative became positive when blood was withdrawn for a second test, and in another two cases the complement-fixation test when repeated showed an increase in the positivity of the test (Table III).

TABLE III—*Changes in Complement-fixation Test*

Case.	Age.	Day of illness when blood was withdrawn.	Result.
A	3½ years.	11	Negative.
		38	Doubtful positive.
		71	Positive.
B	7 months.	6	Negative.
		20	Weak positive.
C	4 years.	45	Weak positive.
		73	Positive.
D	4½ „	14	Weak positive.
		33	Positive.

Group 2: vaccine treated.—Of 43 cases treated with the smooth form of pertussis vaccine, 36, or 83·7 per cent., gave positive complement-fixation reactions.

The average duration of the illness from the onset until the blood was withdrawn was 55·8 days. The average amount of vaccine given to an individual patient up to the time when the blood was withdrawn was 14·75 c.cm. of a vaccine containing 4000 million smooth strain whooping-cough bacilli per c.cm. In this group there were only 4 cases from whom blood had been withdrawn on or before the twenty-first day of illness. Each of these 4 cases gave positive complement-fixation reactions. Of the 39 cases who had blood taken off after the third week of illness 32 gave positive complement-fixation reactions (82·05 per cent.).

Again as in Group 1 it is interesting to note the number of cases with negative complement-fixation reactions in the various age-groups (Table IV).

TABLE IV—*Variation with Age*

Age in years.	Number of cases.	Negative.	
		Number.	Per cent.
0–2	22	5	22·7
2–5	16	2	12·5
5 and over ..	5	0	0

An analysis of the 7 cases with negative complement-fixation tests reveals similar factors to those acting in Group 1, and again the result of each complement-fixation test may have been influenced by one or more factors.

1. Extreme youth: 4 children were less than a year old when the blood was withdrawn.
2. Anticomplementary sera: The sera was anticomplementary in 3 cases, each result being labelled negative.
3. A severe form of whooping-cough: 1 case had severe whooping-cough when the blood was withdrawn.
4. The presence of acute complications: 1 case had broncho-pneumonia when blood was withdrawn.
5. In 2 cases less than the optimum amounts of antigen or sera or both were used, and there were 2 doubtful positives amongst the 7 cases recorded as having negative complement-fixation reactions.

Control series.—In a control group of 37 children, aged 0–5 years, convalescing from broncho-pneumonia and with no previous history of whooping-cough, 36 had negative complement-fixation reactions and 1 gave a "doubtful positive" reaction.

THE INTRADERMAL TEST

In this section the object was to investigate the possible value of the skin test in the diagnosis of whooping-cough, using the complement-fixation test as a control. The blood for the complement-fixation test was withdrawn in each case before the skin test was done. The cases have been divided into two groups. Group A consisted of 43 patients untreated by vaccines, most of whom were under five. These patients had been admitted to the wards with the diagnosis of whooping-cough with or without complications. Group B was composed of 37 patients, aged up to 5, who were convalescing from broncho-pneumonia and had no previous history of whooping-cough. This group has thus been used as a control to Group A of this series, as well as acting as control material for the complement-fixation test.

Group A.—Of the 43 cases 25 were skin tested with Sauer's vaccine, 14 were skin tested with St. Mary's vaccine, 3 were tested with Glaxo vaccine composed of 8000 million organisms per c.cm., and one was skin tested with Kreuger's vaccine. Out of the 43 cases 31 gave positive complement-fixation reactions and, of these 31 cases, 21 gave positive skin tests. Of the 12 cases with negative complement-fixation reactions 9 gave positive skin tests. Altogether 30 out of the 43 cases (69·7 per cent.) gave positive intradermal tests.

Group B.—The antigens used for the skin tests in this group were Sauer's vaccine and Glaxo vaccine containing

the constituents of 8000 million whooping-cough bacilli per c.cm. Each case was tested at the same time with the two vaccines.

Of the 37 cases, 36 gave negative complement-fixation reactions and 1 case had a "doubtful" reaction. In the skin tests 31 cases of the 36 were positive with both Sauer's and Glaxo vaccine. Amongst the remaining 5 cases, 3 gave negative skin tests with both antigens, 1 gave a negative skin test with the Sauer antigen, and a positive skin test with the Glaxo antigen, whilst the other gave a positive skin test with Sauer's vaccine and a negative skin test with the Glaxo vaccine. The case with the doubtful positive complement-fixation reaction gave a positive skin test with both the Sauer and the Glaxo vaccine.

Summary

The complement-fixation test is of value in confirming the clinical diagnosis of whooping-cough. In atypical cases the test may by itself establish the diagnosis of pertussis by conversion from a negative to a positive reaction during the course of the illness.

Although the majority of the patients in this series were admitted in the later stages of the infection, there is evidence from the numbers admitted in the first three weeks of the disease that the complement-fixation test becomes positive early in the infection in a high proportion of cases.

Negative results were most commonly obtained in very young children in whom there seems to be a poor antibody response. Other apparent causes of a negative reaction were short duration of the disease, very severe infection or presence of complications, and anticomplementary sera.

The intradermal test failed to give specific results. A high percentage of patients with whooping-cough gave positive reactions, but so also did a group of control patients with no history of whooping-cough. There was no correlation between the intradermal test and the complement-fixation reaction.

This work was commenced in Belvidere Hospital, Glasgow, in December, 1934, with the kind permission of Dr. A. S. M. Macgregor, medical officer of health for Glasgow, and Dr. Thomas Archibald, medical superintendent. The complement-fixation tests were carried out in the bacteriological department of the Royal Infirmary, Glasgow, under the personal supervision of Dr. Robert Cruickshank, bacteriologist to the Royal Infirmary, to whom I am indebted for animal inoculations and for revision of the text.

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GREENOCK ROYAL INFIRMARY.—At the annual New Year's Day meeting of subscribers to Greenock Royal Infirmary it was announced that the directors had adopted a scheme for extending the Larkfield Hospital to provide 50–60 additional beds. The chairman, Mr. D. N. Ferguson, said the proposed extension would do away with the waiting-list, though they were more fortunate than many hospitals in having only 11 on their list. Various substantial legacies and gifts had been received by the hospital during the year, and the income from all sources had increased. He hoped that the final statement for the year would show that the debit balance that had accumulated during the years of trade depression had almost gone.

NÆVOCARCINOMA OF THE SKIN AND MUCOUS MEMBRANES

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NÆVOCARCINOMATA have for many years interested pathologists because of their colour, and physicians because of their generally fatal result. The many theories put forward about the origin of their pigment and the derivation of their characteristic cells have led to a confused nomenclature, but clinicians are all agreed on their extreme malignancy.

An analysis of 25 cases admitted to the Middlesex Hospital during the years 1928–35, together with some cases of benign melanomata, has been made in order to study the histology, to correlate the histological and clinical types with prognosis, and to emphasise the clinical features. In the discussion on treatment, more recent cases have been included and no attempt has been made to give a statistical survey.

The term "nævocarcinoma" was introduced by Unna to cover the group of malignant tumours previously known as the melanoblastomata. Controversy has raged as to whether these tumours are carcinomata or sarcomata, as they may consist of cells whose appearance suggests epithelial or connective tissue origin (Unna 1893, Ewing 1930, Dawson 1925, and Masson 1926) and some authorities recognise two types, the melanocarcinoma and the melanosarcoma. Both are usually characterised by the presence of pigment, but the problem is complicated by the occurrence of tumours histologically identical but without pigment. Cases have been noted where the primary growth is pigmented whilst the secondary deposit is not, or where the primary tumour is non-pigmented whilst the secondary deposit is deeply coloured.

BENIGN PIGMENTED TUMOURS

Benign pigmented tumours are extremely common; Pack, quoted by Adair (1936), in a careful clinical investigation found that every individual has at least 20 pigmented spots on his person. These spots are important for two reasons—they may cause disfigurement or become malignant.

Disfigurement.—Fifty per cent. of these tumours occur on exposed surfaces of the body—i.e., face, neck, and arms—and the patient seeks advice for cosmetic reasons. The safest and best procedure in these cases is a thorough and clean excision with a scalpel, as there is abundant proof that trauma, in the form of electrodesiccation and burning with carbon dioxide snow, may excite a malignant change. They are not radiosensitive, although a hairy mole may be depilated.

Malignant change.—Twenty per cent. of our cases of nævocarcinomata arose as a malignant change in a previously benign melanoma. As Sampson Handley has pointed out, the chances of a benign melanoma becoming malignant, however, must be very small, at least some thousands to one. The points of practical importance are: (1) Which type is liable to become malignant? (2) The factors exciting malignant

change. (3) The clinical evidence of malignant transformation, since histologically it may be very difficult to be certain whether a mole is benign or malignant.

Types.—In our cases the following clinical types occurred :—

1. A diffuse flat pigmented type.
2. A raised hard nodular type, often papillary.
3. A soft raised nodular type.
4. A hairy circumscribed type.

Site.—The majority of these apparently benign melanomata occurred in the upper half of the body, their sites being: cheek (2 cases), cervico-dorsal region (1 case), upper abdomen (1 case), and sole of the foot (1 case). Of these 5 cases one, the hard raised nodular type with a papillary surface, had progressed to a squamous-celled carcinoma. In this type the cells are differentiated along the line of squamous epithelium and are only secondarily pigmented. There were 3 cases of the soft raised type that became nævocarcinomata; being raised they were subjected to trauma and exposed to constant friction which was probably a potent factor in exciting malignant change. The fifth case was of the diffuse flat type on the upper abdomen, was subjected to friction by tight clothing, and was also a nævocarcinoma.

Signs of malignant change presented themselves in one of the following forms :—

1. Increase in size of the original tumour.
2. Ulceration.
3. Hæmorrhage.
4. Appearance of nodules in the skin around the original tumour.
5. Enlargement of lymph glands without change in the original tumour.

ACQUIRED NÆVOCARCINOMATA

Out of an average of 800 cases of malignant disease seen annually at the Middlesex Hospital during the years 1930 to 1935, there were about 6 cases of nævocarcinoma a year. Their ages varied from 19 to 81, the greatest incidence being the sixth to seventh decades. Both sexes were equally affected. Clinically demonstrable secondary deposits were present in 60 per cent. of the cases when they first sought advice, and one case developed inoperable glands while awaiting admission to hospital. In one case wide-spread metastases made themselves apparent clinically during the 14 days after the surgical removal of the primary growth.

Clinical types :—

1. Nodular, papillary, or warty.
2. Pedunculated.
3. Associated with neurofibromatosis.
4. Ulcerated.
5. Subcutaneous nodular.
6. Glandular enlargement, no primary lesion found.

Some cases are difficult to assess as truly acquired, since the congenital type may be subcutaneous and latent.

Sites.—In our series the acquired nævocarcinomata occurred at random on skin and mucous membranes: face (4 cases), ear (2), palate (1), nasal mucous membrane (1), chest (1), abdomen (2), arm (5), thigh (3), and lower limbs (6). No case of nævocarcinoma occurred in normally pigmented areas, such as the axilla, areola of the nipple, linea nigra, or anal region.

Features.—Of the 25 cases, 8 showed non-pigmented tumours. The ulcerated type commenced as a raised nodule the centre of which broke down to leave an indurated edge. In many, owing to rapid growth, the edge was softer than in the squamous epitheliomata. Some of the non-pigmented clinical types had a slight black rim at the edge of the ulcer which gave the clue to their nature. In some of the other cases there was no central degeneration, a soft, raised, bleeding tumour being exposed when dressings were removed. There were 2 cases in the series associated with multiple nodules on the abdomen and thighs, which followed the course of subcutaneous nerves and were diagnosed clinically as multiple neuro-fibromata. One of these cases had a nodule on the thigh which was cystic and pigmented. There was only one case in which histological examination of an enlarged gland revealed nævocarcinoma and where a primary could not be found.

Histology.—Material consisting of skin and lymphatic glands was examined from 23 cases of nævocarcinoma. Three types of tumour cell were distinguished :—

1. The "squamous" type is named because of its superficial resemblance to the cells of squamous epithelium. The cell is irregular or polygonal in shape with an eosinophilic cytoplasm and nuclei variable in shape and staining intensity, showing mitotic figures.
2. The "spheroidal" type is so named because it resembles cells occurring in spheroidal-celled carcinoma. These cells consist almost entirely of large, pale-staining, reticulated nuclei, often showing mitosis, and a minimum of cytoplasm.
3. The "spindle" type resembles sarcoma cells. The nuclei are irregular in shape and size with mitoses and little cytoplasm.

Two distinctive arrangements of tumour cells were encountered.

The papillary type, in which the tumour cells lay in loose papillary formation, in relation to a connective tissue stroma which appeared to be part of the growth, as distinct from connective tissue of the invaded tissue. This arrangement was largely favoured by the "squamous" type of cell (Fig. 1A).

Closely packed masses of tumour cells with little or no stroma, a formation largely adopted by the "spheroidal" type of cell (Fig. 1B).

Certain growths showed no definite arrangement and were in the nature of a diffuse infiltration. Where there was a definite arrangement in the primary growth it persisted in the lymphatic gland metastases in some cases. The following combinations of cell type and arrangement were met with :—

1. Papillary arrangement of squamous type of cell: 13 cases.
2. Masses of "spheroidal" type of cell: 5 cases.
3. Masses of "squamous" type of cell: 3 cases.
4. Masses of "spindle" type of cell: 2 cases.

Pigmentation.—In the 23 cases 11 tumours were pigmented, and in one case pigment was present in a lymphatic gland metastasis from an apparently non-pigmented primary. The pigment appeared to be deposited in the tumour cells themselves, in the "squamous" and the "spindle" cell types of growths.

Benign pigmented moles.—Examination of sections of benign pigmented moles led to the following conclusions: (1) All three types of cell: "squamous," "spheroidal," and "spindle," occurring in nævo-carcinoma could be recognised. (2) There was no histological difference between cells of the same type in benign and malignant growths, barring the greater frequency of mitosis in the latter. (3) The majority of benign growths showed a mixture of squamous cells in papillary arrangement in the superficial layers with masses of "spheroidal" cells in the deeper layers.

Malignant change in congenital moles.—In 4 of our 25 cases there had been sudden rapid growth of pigmented moles which had been present for 20, 25, 34, and 40 years, a history of trauma being definite in one case. No histological difference could be detected between these growths and those apparently arising de novo (Fig. 2).

Biopsy in doubtful cases.—Darier and Ravaut (Darier 1936) state that a biopsy in a doubtful case should never be performed as the histological picture is difficult to interpret, and the trauma may be a factor in precipitating a malignant change in the tumour. Such cases should be treated as nævocarcinomata.

TREATMENT

Surgery.—The majority of primary tumours were excised with the scalpel or diathermy knife. In all cases where possible, whether there were palpable glands or not, the regional lymphatic glands connected with the primary tumour were excised. All tumours in which a local excision was done recurred either locally or in the neighbouring skin and necessitated a second operation. In some cases the primary tumour, secondary metastases, and the connecting fascial lymphatic channels were excised. In one case of primary nævocarcinoma of the foot, amputation through the lower third of the femur was performed, together with a wide radical dissection of the inguinal glands, being the only means of ensuring complete removal. The glands were not invaded and this case is still alive without evidence of recurrence three years later. In spite of wide excision some cases advanced rapidly.

In a recent case a small congenital mole on the ear which suddenly increased in size was removed locally

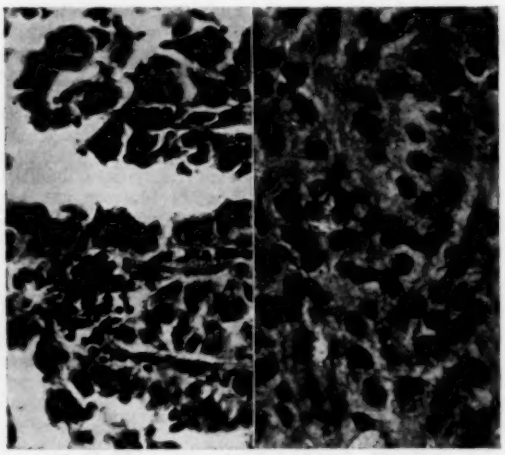

FIG. 1.—(A) Papillary type of nævocarcinoma with "squamous" cells. (B) Closely packed "spheroidal" type of cells.

and proved to be a nævocarcinoma on section. The patient was admitted to hospital immediately and a wide excision of the ear was done, together with an extensive block dissection of the cervical glands; 6 weeks later a recurrence developed in the lymphatic glands of the pre-auricular region and in a gland low in the posterior angle of the posterior cervical triangle.

Radiotherapy.—Isolated instances are recorded in the literature of successful treatment of nævocarcinomata by radiotherapy (Holfelder 1929, Pack 1928, Anderson 1935, McEuen 1930). The French school of dermatologists, however, state that the tumour is so radioresistant that radiotherapy is contra-indicated. Even surgical excision is condemned as being insufficient and as leading to a false sense

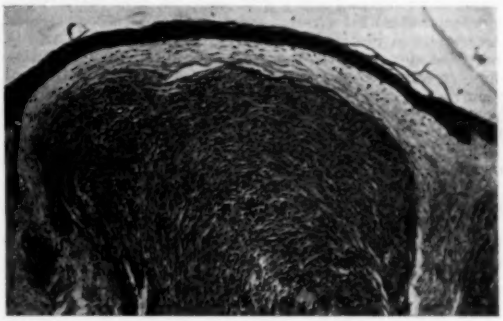

FIG. 2.—Showing squamous cells in papillary arrangement in superficial layers and spheroidal cells in the deeper layers.

of security, and they advise treatment by diathermy coagulation. We have found some cases to be sensitive to gamma rays of radium and to X rays. The methods of application depended upon the site of the primary tumour.

CASE 1.—Female, aged 35, with 6 months' history of slightly pigmented raised tumour on dorsal surface of the big toe with enlarged glands in the groin. The primary was treated by a surface application of radium on a Nidrose applicator, a dose of 6000 *r* units being given in 10 days. The reaction proceeded to a moist desquamation with rapid healing and disappearance of the original tumour. The inguinal glands were excised and a post-operative course of deep X ray therapy given. There was no recurrence to date, 9 months later.

CASE 2.—Male, aged 26, with 9 months' history of an ulcerated growth, fixed to the hard palate and alveolus. Treated by surface application of radium on a dental applicator receiving a dose of 7000 *r* in 10 days, together with 118 hours by a 1 gramme unit to the neck in 32 days. The primary lesion healed satisfactorily and there is no recurrence to date, 8 months later.

CASE 3.—Male, aged 63, with 3 months' history of an ulcer on the thigh with a recent lump in the groin. The primary was treated by deep X ray therapy receiving a dose of 8600 *r* in 6 weeks, 190 kv, 6 ma; distance 40 cm. The primary lesion healed rapidly while undergoing treatment, but recurred within three months on the margin of X ray pigmentation.

Of other cases treated, 1 case with fixed inguinal glands became operable, 1 case with a nævocarcinoma of the nasal mucous membrane responded well to teleradium therapy, and 1 case with a large recurrence in the dorsal region responded well to surface radium treatment; the tumour became smaller and flatter and ultimately disappeared. Many cases are definitely radioresistant. No criterion of radio-sensitivity has been found by histological examinations except that the non-pigmented tumours appear to be more sensitive than the pigmented. If pigmentation is an index of cell activity and therefore differentiation, it would agree with the suggestion that non-pigmented tumours, being undifferentiated, are more malignant (see prognosis) and possibly more radiosensitive.

PROGNOSIS

The prognosis of nævocarcinoma is generally considered to be very poor. All our five undoubted "congenital" cases are alive and well without

recurrence, 1 for 5 years, 3 for 2 years and 1 for 1 year after treatment.

Of the 20 "acquired cases," 15 are dead; 1, 7 years after treatment, from senility; 1 after Cæsarean section for spinal metastases 2 months after excision of the nævocarcinoma, 8 cases in the first 2 years after the onset of the illness, and 4 of these in the first year; while the remainder died within 5 years. All these cases received treatment in the form of surgery or radiotherapy, and in one case alone was the disease so advanced that palliative surgery only was attempted. In 3 cases there were local recurrences in the first year, and in 2 cases in the second year after treatment. In 2 of these cases the recurrence was re-excised more radically but recurred again within 12 months. In 2 cases inoperable glandular metastases occurred within 6 weeks of seeking medical advice.

Of the 5 cases who are still alive the survival-rate is as follows: 1 case, 7 years; 1 case, 6 years; 2 cases, 4 years; and 1 case, 2 years. In 2 of these cases recurrences occurred in the first year after treatment and received yet more radical surgical treatment.

As Ravaut points out the results of treatment vary with the stage of the disease at the time the treatment is applied. If the disease is local and the treatment radical, the results are excellent, and even if the glands have been invaded there is still a chance to eliminate the disease as dissemination occurs by the lymphatic system and blood dissemination is rare.

Relation of histology to prognosis.—Certain conclusions may be drawn from Tables I and II embodying length of history, survival time, and histology.

TABLE I

Cases which Died within 3 years after Treatment

Case.	Length of history.	Survival.	Histology.	Pigment.
1	8 mths.	7 mths.	Papillary squamous.	0
2	?	10 mths.	Papillary squamous.	0
3	6 wks.	Under 1 yr.	Papillary squamous.	0
4	6 wks.	Under 1 yr.	Papillary squamous.	0
5	3 mths.	Under 1 yr.	Masses squamous.	0
6	7 mths.	Under 1 yr.	Papillary squamous.	+
7	?	Under 1 yr.	Papillary spheroidal.	+
8	1 mth.	10 mths.	Papillary squamous.	0
9	4 mths.	3 yrs.	Papillary squamous.	0
10	?	3 yrs.	Masses squamous.	+
11	Few mths.	3 yrs.	Masses squamous.	0

TABLE II

Cases, Congenital and Acquired, which Survived 3 years without Recurrence

18	8 mths.	4 yrs.	Squamous, no arrangement.	+
19	18 mths.	4½ yrs.	Papillary squamous and masses spindle.	0
20	20 yrs. (cong.)	5 yrs.	Masses spheroidal.	+
21	6 mths.	6 yrs.	Masses spheroidal.	+
22	6 wks.	7 yrs.	Masses spheroidal.	+

Thus of the 11 cases that died, 8 had non-pigmented growths and 10 had growths of the squamous type of cell, of which 7 were in papillary arrangements. Of the 5 cases which survived 3 years or more without recurrence 4 had pigmented growths, and the fifth case had glandular metastases which were pigmented, although the primary growth was apparently non-pigmented. Growths of the "masses of spheroidal cell" type occurred in 3 of the 5 cases, as contrasted with only one spheroidal cell tumour in the 11 cases that died. In this connexion it is interesting to note that "spheroidal" cells are predominant in the deeper parts of the benign pigmented moles, as mentioned above.

Although the series of cases is small the following suggestions are made: (1) That the non-pigmented papillary "squamous" cell growth is the most malignant. (2) That the pigmented masses of "spheroidal" cell growth is the least malignant. (3) The presence of pigment in a growth appears, ceteris paribus, to be more favourable than its absence.

CONCLUSIONS

A review of the 25 cases of nævocarcinoma at our disposal has impressed upon us that improvement in results can only be achieved by attention to the following points:—

Prophylaxis.—The removal with a scalpel of outgrowing pigmented congenital tumours exposed to friction by shoes, clothing, or toilet.

Urgency of treatment.—The original tumour has been known to double its size within 48 hours and the disease should be included among the "surgical emergencies."

Radical surgical removal.—However small the primary lesion, a wide excision with at least 2 in. of normal skin, together with an extensive radical dissection of the lymphatic glands and fascia is essential. Where this necessitates amputation of a limb it should be advised without hesitation.

Radiation treatment.—The fact that many tumours are radiosensitive, although no criterion of sensitivity has been found, seems to us sufficient argument that a full carcinoma-lethal dose should be applied in all cases, and even where radical surgery is possible this course of treatment should be given as a post-operative measure. We are of opinion that radiotherapy has much wider scope in the treatment of nævocarcinoma than its limitation to advanced and inaccessible cases.

Careful and frequent post-operative observation.

Our thanks are due to the members of the honorary surgical staff of the Middlesex Hospital and to Prof. James McIntosh, director of the Bland-Sutton Institute of Pathology for allowing us to study these cases.

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FUCHS SERUM PROTEOLYSIS TEST FOR MALIGNANCY

A REPORT OF 170 EXAMINATIONS

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MOST of the serodiagnostic methods devised for detecting malignant disease fall into one of the following groups:—

1. Those involving complement fixation and related phenomena.
2. Those involving flocculation or separation of protein or other elements by various reagents.
3. Observations utilising injections of vaccine types of extracts.

4. Tests involving analyses for specific chemical constituents of serum—e.g., cholesterol and cholesterol esters, fibrin, fatty acids, magnesium.

5. Physico-chemical methods involving measurement of *p*H, surface tension, osmotic resistance, and electric charge determination on corpuscles, coagulation time, sedimentation-rate, &c.

6. Reactions dependent on enzyme changes—e.g., Abderhalden's reaction and modifications, the Freund-Kaminer cell cytolysis test, the lipolysis test of Shaw Mackenzie, and the proteolysis reaction of Fuchs.

Some of these tests have proved useless in practice; others, while yielding a variable proportion of correct results, are far from specific and probably indicate the presence of cachexia, anæmia, and toxæmia rather than the cancer which has caused them.

It seemed to me probable that the reactions which depend on enzyme changes were the most likely to afford means of biochemical detection of malignant processes. Some work on the augmentation of pancreatic lipolysis by serum (Woodhouse, 1932) having yielded no satisfactory results I decided to try the protein enzyme test described by Fuchs (1926), which seemed to offer greater possibilities than any other. It is true that the Abderhalden reaction in its original form, whether carried out by chemical or physico-chemical methods, has been adversely criticised, but actually the Fuchs test depends on a different aspect of the immunological thesis in that the observed proteolysis is produced by the interaction of cancer serum on non-cancer protein or vice versa—i.e., the reaction is heterologous in type.

In 1930 Wright and Wolf investigated many of the details of the test. Of over 100 cases examined about 86 per cent. gave correct results, and in 20 non-malignant cases the result was correctly negative in every instance. Cadness and Wolf (1934) carried out further observations on the influence of such factors as radiotherapy, heat, and alcohol. Fuchs and Devrient (1932) produced evidence that the reaction is dependent on a true antigen-antibody interrelationship, and this was further confirmed by Fuchs and Kowarzyk in 1933, who found that intravenous injections of homologous serum containing cancer "antigen" caused the serum of normal men to give a positive Fuchs reaction over a period of six months. Falkenhausen (1932) carried out the test in 80 cases without previous knowledge of the clinical findings, and obtained correct results with all sera. Chrometzka and Gottlebe (1932) investigated 60 specimens; 26 of them were from cancer patients, and 24 of these proved positive, while all the rest were negative. They were able to enhance the proteolysis by using ultra-filtered sera, and obtained 22 correct results in a corresponding number of samples treated in that way. They concluded that this reaction was the most dependable serum diagnostic test so far devised for cancer. In 125 patients (excluding œsophagus cases) Jedlicka and Weichherz in 1934 obtained 93 per cent. correct results by the Fuchs reaction, and Kafka (1934) in 56 patients had 51 correct (91 per cent.), while 39 non-cancerous sera yielded 100 per cent. correct results. In 1933 Bing stated that, in all, some 3600 tests have been carried out by various investigators using the Fuchs reaction, and that correspondence with the clinical findings of 90–92 per cent. was observed.

Some of the difficulties regarding the test were removed by Fuchs (1932 a and b), who showed that the fibrin substrate might be replaced by the dried protein coagulum obtained by the trichloracetic acid precipitation of suitable serum. The technique was further simplified by the application of a colorimetric method of estimation of the rest nitrogen (Fuchs and Falkenhausen 1932) instead of the original iodometric technique.

METHODS

Fuchs (1936) has lately described his test in detail, and this should be followed precisely; but as my own work was almost completed before his latest description appeared I will give an account of the method as I actually employed it.

The substrates were produced from the serum of healthy persons or of known cancer patients, the proteins being precipitated with 10 parts of 2½ per cent. trichloracetic acid and washed several times with trichloracetic acid followed by distilled water. They were dried at 40° C., powdered and tested for their proteolytic reaction on known normal and cancerous sera. A number of satisfactory proteins have been tested, but two cancer and two normal preparations have been utilised for practically the whole of the tests described in this paper.

For the diagnostic tests 10 c.cm. samples of blood were withdrawn from the patients by a sterile syringe after 12 hours' fast, and exactly 0·5 c.cm. of the clear, centrifuged, non-hæmolysed serum placed in three similar tubes 3½ in. by ½ in. 5 mg. of the protein substrates of normal and cancer types respectively were weighed into two of these. This quantity has been shown to be a large excess so that exact weighing is not necessary. The three samples were incubated at 40° C. in a moist chamber for 24 hours and the proteins then precipitated by adding 3·0 c.cm. of water and 0·50 c.cm. of 25 per cent. trichloracetic acid. After standing for 20 minutes and filtering through a hard filter paper, 2·0 c.cm. of the clear filtrate was digested with 0·5 c.cm. phosphoric-sulphuric acid mixture (300 c.cm. 85 per cent. phosphoric acid + 100 c.cm. pure sulphuric + 50 c.cm. 5 per cent. copper sulphate solution), and then the non-protein nitrogen estimated by adding 14·5 c.cm. of water and 10 c.cm. of Nessler solution and matching with a suitable ammonium sulphate standard in the colorimeter. All these quantities were measured by means of carefully standardised pipettes and accidental contamination of all glassware was scrupulously avoided. Since the significant change is not less than 3 mg. per 100 c.cm. the proteolysis is measured with sufficient accuracy by this means, provided that the processes are carried in identical fashion in all tests. Particularly in the nesslerisation process is it necessary to avoid the presence of the slightest turbidity in the liquid. The use of porous pot is undesirable for preventing percussion in the combustion process, and the addition of a few fragments of pure broken silica was found to be efficacious.

The Nessler solution was prepared from mercury, iodine, and potassium iodide, and the alkalinity carefully standardised so that in the final colorising process the product was clear and remained free from deposit or cloud for at least half an hour. The complete combustion and nesslerisation operations were carried out in the same Pyrex glass tubes (8 in. by 1 in.), and there was thus no error due to transference.

The colour comparison was carried out in a dark-room, employing a lamp house and blue screen; the standards for matching were prepared from pure ammonium sulphate solution, 0·1886 g. per litre. For comparisons with sera containing the normal non-protein nitrogen value, 2·0 c.cm. of this was utilised in a final volume 25 c.cm.

The interpretation of the analyses is based on the fact that serum from non-malignant persons gives zero or slight proteolysis with normal human blood protein but a greater proteolysis with the blood protein from cancer patients. Inversely a cancer serum causes a much greater proteolysis of normal protein. It is necessary to exclude tuberculosis, syphilis, and certain chronic regenerative processes from the possibilities, since these conditions may give proteolytic reactions on normal protein. They may be differentiated from the true "malignant reactions" by conducting "blanks" with "syphilitic," "tuberculous" protein, &c.

RESULTS

In the majority of the pathological cases investigated, the clinical diagnosis was not known until after the test was completed; in many cases a considerable time elapsed before the tentative diagnosis was finally confirmed.

A total of 170 sera have been examined by this method, and up to the present the diagnosis in 120 is sufficiently established (usually by operation, histological or post-mortem examination) for comparison with the serum reaction. These comparisons are set out in three Tables, comprising the non-malignant cases (Table I), the untreated malignant cases (Table II), and the malignant cases previously treated by irradiation (Table III). These serve to indicate the variety and types of disease in the patients examined and the measure of the proteolysis encountered in all cases clinically diagnosed.

The following are protocols of two tests with normal and cancer serum respectively:—

TABLE I.—*Non-malignant Cases*

Clinical diagnosis.	Mg. N_2 per 100 c.cm. (*a*)	(*b*)	(*c*)	Reaction.
Healthy normal	49	50	55	−
? Rodent ulcer (section normal)	25	28	33	−
Menopausal hæmorrhage	26	30	35	−
Ulcer of throat	35	40	46	−
P.M. no malignancy found (pneumonia)	58	71	65	+
Simple tumour of ventricle (non-malignant)	37	37	42	−
	32	35	38	−
Normal healthy	29	32	36	−
" "	29	30	—	−
Gonorrhœa	27	29	34	−
Normal healthy	17	20	25	−
Ulcer soft palate	35	38	42	−
Normal healthy	30	35	40	−
Papilloma of tongue (section normal)	19	21	24	−
Normal healthy	14	17	20	−
" "	18	21	24	−
" "	34	36	39	−
" "	26	29	32	−
" "	32	34	39	−
Diabetes	26	27	—	−
Lead poisoning	49	64	68	+
Cardiac disease	90	92	98	−
Hæmolytic jaundice	33	37	42	−
Arthritis	31	33	37	−
Gastric ulcer	24	27	33	−
Pernicious anæmia	18	22	26	−
Gastric ulcer	16	18	24	−
Colitis	24	28	33	−
Gastric ulcer (G.P.I.)	17	19	24	−
Menopausal hæmorrhage	26	28	32	−
No neoplasm found P.M.	35	48	40	+
Asthma, erysipelas	25	26	30	−
Vaginal hæmorrhage (no sign of neoplasm)	125	130	138	−
Diabetes	64	72	70	+
Cerebral degeneration	35	36	42	−
Ovarian cyst	35	38	43	−
Ulcer of stomach	32	35	39	−
Chronic cholecystitis	33	35	40	−
Menorrhagia	26	30	35	−
Diverticulitis	30	30	36	−
Normal healthy	36	38	40	−
Pernicious anæmia	22	22	26	−
Venereal disease				

Tables I, II, and III: (*a*), (*b*), (*c*) = Rest nitrogen per 100 c.cm. of serum—
(*a*) After incubation alone.
(*b*) After incubation with normal protein substrate.
(*c*) After incubation with cancer protein substrate.
P.M. = post mortem.

PROTOCOL 1

(a)—Rest nitrogen after incubation at 40° C. for 24 hours.

2·0 c.cm. filtrate (= 0·25 c.cm. serum).
Final volume for Nessler comparison = 25 c.cm.
Standard ammonium sulphate = 2·0 c.cm. = 0·08 mg.
Volume of standard solution = 25 c.cm.
Colorimetric readings { standard = 20·0 mm. / solution = 18·3 mm.

$$\therefore \text{Rest nitrogen} = 0{\cdot}08 \times \frac{100}{0{\cdot}25} \times \frac{20}{18{\cdot}3}$$

= 35 mg. per 100 c.cm.

TABLE II.—*Malignant Cases*

Clinical diagnosis.	Mg. N_2 per 100 c.cm. (*a*)	(*b*)	(*c*)	Reaction.
Sarcoma of femur	30	64	—	+
Carcinoma of breast (glands)	32	58	—	+
" breast	25	28	29	−
Epithelioma of tongue	28	38	29	+
Ditto (recurrent)	36	53	39	+
Epithelioma of mouth	30	49	—	+
Carcinoma of œsophagus (glands)	28	43	32	+
" breast (recurrent)	27	34	29	+
" bronchus, secondary pancreas	40	54	44	+
Epithelioma of tongue	37	46	34	+
Carcinoma of breast	36	43	38	+
Recurrent carcinoma of rectum	29	40	—	+
Carcinoma of ovary	38	49	42	+
Malignant growth in pelvis	43	58	46	+
Epithelioma of anal canal, glands in groin	35	53	—	+
Carcinoma of breast (recurrent)	25	30·5	28	±
" cervix	34	40	34	+
Epithelioma of nipple	44	49	45	+
" penis	21	30	22	+
Carcinoma of stomach	34	37	37	−
Epithelioma of tongue	37	43	40	+
" lip	29	38	30	+
Colloid carcinoma of breast	31	41	32	+
Bilateral carcinoma of breast	32	41	34	+
Epithelioma of tongue	37	35·6	37	±
Recurrent carcinoma of breast	39	48	39	+
Carcinoma of lip (early)	44	49·8	47	±
" breast	34	50	39	+
Ditto (glands in neck)	34	44	36	+
Carcinoma of breast	19	29	22	+
" "	56	64	60	+
Ditto (recurrent, glands in axilla)	37	52	38	+
Carcinoma of cervix	36	78	40	+
Epithelioma of hand	38	45	40	+
Carcinoma of cervix	98	40	96	+
Adenocarcinoma of ovary	23	29	23	+
Carcinoma of stomach	41	52	43	+
" colon	48	55	50	+
" stomach	34	45	37	+
Tumour (malignant) of spinal cord	56	66	59	+
Carcinoma of stomach	24	32	26	+
Inoperable widespread carcinoma	35	48	40	+
Epithelioma of vulva	30	39	31	+
Carcinoma of œsophagus	25	53	30	+
" lung	30	34	35	−
" stomach	25	33	—	+
" "	35	53	—	+
" ventricle	30	37	32	+
" stomach	30	37	30	+
" breast	28	34	28	+
Ditto (secondaries in spine)	29	34	29	+
Recurrent carcinoma of breast	34	38	36	+
Epithelioma, secondaries in groin	32	40	36	+
Carcinoma of cervix	27	34	29	+
" head of pancreas	36	59	46	+
Epithelioma of lip	34	56	40	+

N.B.—It has been made a rule that for a definite diagnosis of malignancy the nitrogen difference with the normal substrate shall be at least 100 per cent. greater than the corresponding difference with the cancer substrate.

(b)—Rest nitrogen after incubation with normal protein substrate (*N*1).

Quantities as in (*a*).
Colorimetric readings { standard = 20·0 mm. / solution = 17·8 mm.

$$\therefore \text{Rest nitrogen} = 0{\cdot}08 \times \frac{100}{0{\cdot}25} \times \frac{20}{17{\cdot}8}$$

= 36 mg. per 100 c.cm.

(c)—Rest nitrogen after incubation with cancer protein substrate (*C*1).

Quantities as before.
Colorimetric readings { standard = 20·0 mm. / solution = 15·3 mm.

$$\therefore \text{Rest nitrogen} = 0{\cdot}08 \times \frac{100}{0{\cdot}25} \times \frac{20}{15{\cdot}3}$$

= 42 mg. per 100 c.cm.

Therefore:—

Proteolysis due to action with { normal substrate = 1·0 / cancer = 7·0 } mg. per 100 c.cm.

Therefore reaction is non-malignant in type. (Case = ovarian cyst.)

TABLE III.—*Radiated Cases*

Clinical diagnosis.	Mg. N_2 per 100 c.cm. (a)	(b)	(c)	Reaction.
Carcinoma of cervix	30	40	36	±
Sarcoma of arm	35	38	38	−
Epithelioma of ear	36	40	42	−
Recurrent carcinoma of breast	27	29	27	−
Carcinoma of breast	31	34	34	−
" "	30	35	—	−
Epithelioma of ear	30	31	32	−
" lip	28	29	29	−
Carcinoma of breast (amputated previously)	40	43	46	−
Epithelioma of tongue (apparently cured)	30	33	36	−
Epithelioma of lip (12 months previously, apparently cured)	23	27	27	−
Rodent ulcer	19	20	20	−
Carcinoma of breast	34	38	35	? −
" cervix	28	29	—	−
" breast	30	35	—	−
" cervix	21	24	26	−
" "	37	40	41	−
" "	125	130	130	−
Epithelioma of lip	25	22	23	−
" "	19	22	23	−
Adenocarcinoma of thyroid	40	47	43	+
Epithelioma of face	33	34	36	−

PROTOCOL 2

(*a*)—*Rest nitrogen after incubation at 40° C. for 24 hours.*

All quantities as in Protocol 1.

Colorimetric readings { standard = 20·0 mm. / solution = 20·0 mm.

$$\therefore \text{Rest nitrogen} = 0{\cdot}08 \times \frac{100}{25} \times \frac{20{\cdot}0}{20{\cdot}0}$$

$$= 35 \text{ mg. per } 100 \text{ c.cm.}$$

(*b*)—*Rest nitrogen after incubation with normal protein substrate* (*N*2).

All quantities as in above.

Colorimetric readings { standard = 20·0 mm. / solution = 15·7 mm.

$$\therefore \text{Rest nitrogen} = 32 \times \frac{20}{15{\cdot}7}$$

$$= 40{\cdot}8 \text{ mg. per } 100 \text{ c.cm.}$$

(*c*)—*Rest nitrogen after incubation with cancer protein substrate* (*C*1).

All quantities as in above.

Colorimetric readings { standard = 20·0 mm. / solution = 18·7 mm.

$$\therefore \text{Rest nitrogen} = 32 \times \frac{20}{18{\cdot}7}$$

$$= 34{\cdot}2 \text{ mg. per } 100 \text{ c.cm.}$$

Therefore :—

Proteolysis due { normal substrate = 8·8 / cancer " = 2·2 } mg. per 100 c.cm.

Therefore reaction is malignant in type. (Case=carcinoma mammæ.)

From the Tables it will be seen that the following results have been obtained :—

Total cases	170	
Cases with known clinical diagnosis	120	
Malignant cases correct	50/53	= 94%
Non-malignant cases correct	38/42	= 90·5%
Indefinite reactions	3	
Total correct results (untreated only)	88/95	= 92·6%
Radiated cases (2 positive only)	22	

It is of interest that the proteolysis test has been positive in external epitheliomas where the extent of the lesions was not great. The reaction should, therefore, be of help in relatively early cases of internal cancer also; on the other hand it is not to be expected that "precancerous" conditions will be revealed. The results are, however, definitely encouraging and corroborate the conclusion of Bing and Marangos (1934) that the Fuchs reaction is the most reliable of the serum methods based upon quantitative determinations.

SUMMARY

In 53 malignant cases examined by the Fuchs proteolysis test 50 correct results were obtained. The test also gave correct results in 38 of 42 non-malignant cases. The serum from patients which had previously received irradiation treatment gave negative reactions to normal protein in almost every instance.

My thanks are due to the honorary staff and officers of the Birmingham United Hospital (General Hospital) for coöperation and facilities in obtaining the blood samples and for notes on the cases investigated. The work has been carried out under auspices of the British Empire Cancer Campaign (Birmingham branch).

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THE INTRACRANIAL PRESSURE DURING BARBITAL NARCOSIS

BY J. STEPHEN HORSLEY, M.R.C.S. Eng.

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A STRIKING contrast is presented by the raised intracranial pressure of natural sleep and the lowered pressure during barbital narcosis. This phenomenon was described by Butler (1936), who based his observations on a study of three cases under Evipan sodium anæsthesia. It is of interest to confirm and elaborate these observations. Three questions at once become apparent: Is the pressure effect constant? Is it dependant on depth of narcosis? Is it common to all barbitals? These can be answered only by a longer series of controlled experiments. Earlier reports of similar investigations are of limited value in that they fail to differentiate between partial and full narcosis. For this reason the report of Epstein and Marvin (1933) is misleading in stating that Nembutal has no effect on cerebro-spinal fluid (C.S.F.) pressure. Actually this is true only with small doses; it will be shown that full nembutal narcosis produces a profound fall in C.S.F. pressure. Furthermore it will be shown that this effect is not specific to evipan, but is in fact common to various isomers of barbital.

METHOD

The necessary experimental conditions were fulfilled in administering intravenous barbital to a series of one hundred coöperating patients.

In each case lumber puncture was performed in the left lateral position with the head supported at the same level as the lumbar spine. Pressures were measured with

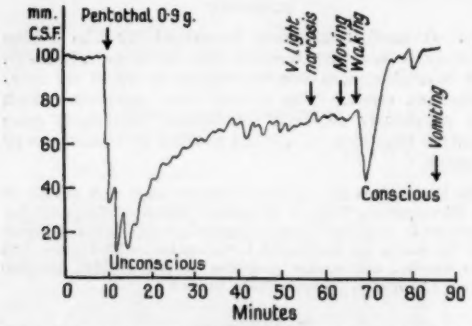

FIG. 1.—Typical pentothal effect showing abrupt fall of 90 mm. of C.S.F. at moment of unconsciousness and a well-marked secondary fall on waking.

a vertical glass-tube manometer fitted to a special needle. Each observation was continued for a period of ½–3 hours and the readings were plotted at 30-second intervals on a graph. The punctures were performed without an anæsthetic except in certain apprehensive patients who received a local injection of percaine. In many cases there were initial fluctuations in pressure from changes in postural tension. For this reason narcosis was not induced until the pressure in the manometer became steady. The barbital solution was then injected by the accepted technique until the onset of unconsciousness.

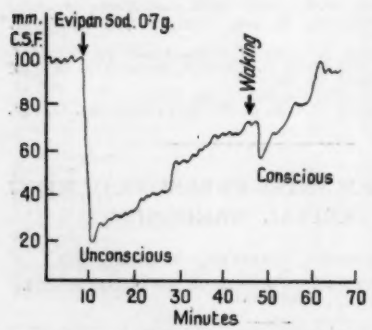

FIG. 2.—Same effect with evipan showing abrupt primary fall and a slight secondary fall.

RESULTS

The effect of narcosis was an abrupt fall in the C.S.F. pressure to about half its previous level (Figs. 1 and 2). This fall either preceded or accompanied loss of consciousness. It was constant and indicative of full narcosis. Cautious over-dosage produced a more profound fall of C.S.F., many cases reaching zero, and two showed negative pressures (Fig. 3). Conversely the administration of a subhypnotic dose of barbital failed to produce any significant change in C.S.F. pressure.

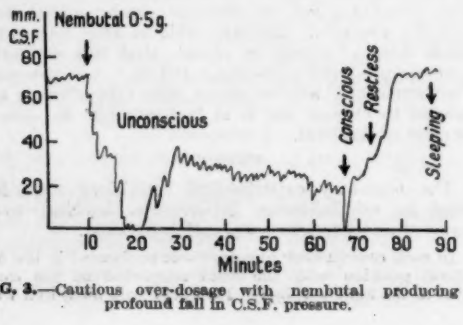

FIG. 3.—Cautious over-dosage with nembutal producing a profound fall in C.S.F. pressure.

In most cases the pressure rose slowly during narcosis but failed to reach its original level until the return of consciousness. In more than half the cases there was a distinct second fall at the moment of waking. Its exact physiological significance is uncertain, but it appears to be connected closely with the central neural control of sleep. The inference is that intracranial pressure is controlled by a central hypothalamic mechanism.

Paradoxical Effect. — In the whole series only one case reacted to barbital with an atypical pressure phenomenon. This peculiarity was enhanced by an exceptionally brief narcosis. The effect of injecting intravenously 0·5 gramme of Pentothal was an immediate rise in pressure from 120 to 295 mm. C.S.F. (Fig. 4). This peak coincided with unconsciousness and muscular relaxation. There was no apparent venous congestion or respiratory obstruction which would account for the raised pressure. It is of complementary interest that within three minutes the patient was awake and alert. Repeated observations with evipan and pentothal showed the same effect. The only other factor of likely relevance is that this patient suffered from idiopathic epilepsy. The causal connexion is obscure but it is reasonable to

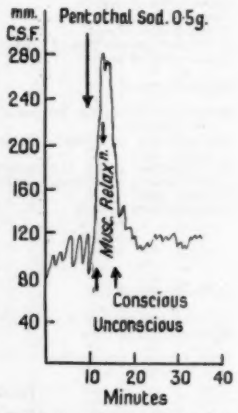

FIG. 4.—Parodoxical effect of pentothal in an epileptic.

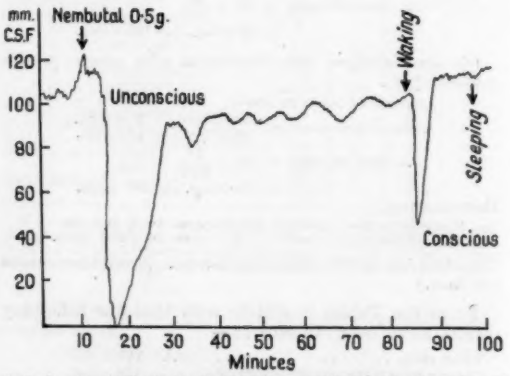

FIG. 5.—Typical effect of injecting nembutal at the rate of 1 c.cm. per minute. Both primary and secondary falls are well marked.

postulate that the pathological changes sometimes found in idiopathic epilepsy might also involve the neural centres for sleep and intracranial pressure.

COMPARISON OF BARBITALS

The 100 pressure effects observed showed a remarkable uniformity. It is of greater significance that this uniformity occurred not only with evipan but with four different barbitals. The series comprised 30 cases of narcosis with nembutal, 30 with evipan, 30 with pentothal, and 10 with Soneryl sodium. Consideration of these cases permits certain tentative conclusions of which the most definite is that the

pressure phenomenon is constant and coincides closely with the hypnotic effect of the particular barbital. This was most pronounced in those cases that received nembutal by very slow intravenous injection (Fig. 5). The pressure would remain steady during the stage of drowsiness and yawning. Then, usually when about 7 c.cm. had been injected, a steep fall of C.S.F. would accompany the sudden loss of consciousness.

The effects of barbital on the pulse, respiration, and blood pressure were studied and found to vary independently of the C.S.F. pressure. Finally a study of "evipan jactitations" and "pentothal clonus" showed that these phenomena were unrelated to the C.S.F. pressure.

SUMMARY

(1) A C.S.F. pressure effect is described in 100 cases in which there was an abrupt fall at the onset of narcosis, succeeded by a slow rise, with a second fall at the moment of waking.

(2) The effect is common to various barbitals: nembutal, evipan sodium, pentothal sodium, and soneryl sodium.

(3) It is constant in 99 per cent. of cases—the single exception being paradoxical.

(4) It depends on full narcosis, and is absent with subhypnotic doses of barbital.

(5) It is suggested that C.S.F. pressure is controlled by a central neural mechanism.

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Clinical and Laboratory Notes

A CASE OF LANDRY'S PARALYSIS

BY A. V. RUSSELL, B.A. Camb., M.B. Liverp.

LANDRY'S paralysis is described as beginning with weakness of the legs which often progresses rapidly to complete paralysis. Trunk muscles are next affected, and then, within a few days or even hours, the arms. The neck muscles are next attacked, and finally, the muscles of articulation, deglutition, and respiration. Reflexes are lost, but muscles neither waste nor show electrical changes. Sensory symptoms are variable, and sensation is usually intact, though there is sometimes tingling, numbness, and hyperæsthesia. The disease is very often fatal.

A girl of 20 was brought to me complaining of feeling tired, of numbness and tinging in her hands and feet, of an occasional sensation as though a ball was rising in her throat, and of a feeling of depression which made her cry. She looked healthy and athletic. Her knee- and arm-jerks were exaggerated; the pupils reacted briskly to light; she had slight tremor of the hands, and her numbness and tingling appeared to be of the glove-and-stocking type. Her hands and feet were cold, the pulse-rate 72 per minute, the temperature subnormal, the tongue clean, the throat healthy, and the heart and breath sounds normal. She seemed depressed, but not unduly emotional. I thought the case was one of nervous debility, gave her a bromide and valerian mixture, and told her to lead as normal and cheerful a life as possible.

Two days later I was called urgently about 8 P.M. She had been taken to a point-to-point meeting that day (which I shall call the first of her illness) and there, after a time, her legs had failed her. On reaching home it was found that her legs had become useless; she could not walk even with assistance. When I saw her the knee- and ankle-jerks were absent; the Babinski reflex was slight and doubtfully flexor. She could just move the toes, the ankles very slightly, and her knees and thighs not at all. The abdominal reflexes were hard to elicit, the arm-jerks brisk, and the eyes reacted normally to light. Temperature 97° F.; pulse-rate 84. She said she had "pins and needles" in her lower limbs, but could feel me touching them with a piece of cotton-wool, and could appreciate the difference between the point and head of a pin lightly applied to them.

There was no history of a recent attack of influenza or of sore-throat, and no indication of alcoholism or of contact with any form of nerve poison; there was no blue line on her gums, and her throat still appeared normal. I called in a consultant colleague and when he arrived about forty minutes later she was no longer able to move her ankles or toes, and her lower limbs were flaccid and powerless. Nevertheless she was curiously placid and undisturbed. She was taken at once into a nursing-home and on lumbar puncture cerebro-spinal fluid came out under considerable pressure—unluckily contaminated by several drops of blood.

The course of events thereafter was as follows: *Second day.* Abdominal reflexes abolished; weakness and tingling in hands. *Third day.* Arm-jerks absent; patient just able to move arms, but unable even to hold a spoon. *Fourth day.* Arms and hands quite paralysed; slight pain and stiffness in neck; pupil reflexes sluggish. Blood count showed:—

Red cells ..	4,170,000 per c.cm.	Polymorphonuclears	76 %
White cells ..	14,100 ,, ,,	Lymphocytes ..	22 %
Hæmoglobin ..	.. .. 73 %	Monocytes	1 %
Colour-index ..	.. .. 0·87	Eosinophils	Nil.
		Basophils	1 %

No morphological abnormalities of red or white cells.

On the *sixth day* she complained that she could not move her head on the pillow, that she saw double, and had some difficulty in swallowing. Her face was expressionless; she spoke in a dull, slow voice, seemed drowsy, and took a long time to answer questions. The eyelids drooped, and the pupils reacted to light very slightly, if at all. During all this time she had been very constipated, and found it difficult to pass water. After the third day she had an enema every day for a week, but catheterisation was only necessary once—on the fourth day. *Seventh day.* Though her face still lacked expression and she continued to be drowsy, there was some improvement in swallowing; she could move her head very slightly from side to side.

Eighth day. Some embarrassment in respiration, which fortunately soon passed off. *Ninth day.* Slight return of movement in hands and fingers, and increased movement of head and neck; face still expressionless; drowsiness and diplopia still present. *Eleventh day.* Much more movement of hands possible, facial expression more alert, head moved easily from side to side on the pillow; swallowing without difficulty; left abdominal reflex returned. *Twelfth day.* Arms moved with some difficulty; patient said they felt extremely heavy and tingled. *Eighteenth day.* Arms moving fairly well; hand-clasp weak. Could move feet a little, and was nearly able to lift head from pillow. Double vision had gone; pupil reflexes normal; abdominal reflexes normal. Massage and electrical stimulation of muscles now begun. *Twenty-fourth day.* Feet and ankles moving much better; able to move knees slightly. *Twenty-fifth day.* Slight knee-jerk response.

From now on progress towards recovery was fairly steady, though on the thirty-fourth day, after sitting up in a chair, there was a return of paresis in both hands, and the patient complained of a tingling sensation in her face; this lasted for four days. She began to walk with assistance on the forty-second day, and at the end of eight weeks was getting about by herself with a stick. Save that she still had a weak hand-clasp and was easily tired, could be considered almost recovered. The illness was apyrexial throughout.

Lumbar puncture was performed every day for the first week, every other day till the eighteenth day, once

again on the twenty-fourth day, and a final puncture on the thirty-fifth day after the return of paresis in the hands.

The first sample of cerebro-spinal fluid was blood-stained, but cultures yielded no growth, protein was 500 mg. per 100 c.cm. globulin in excess, chlorides 0·71 per cent., sugar 0·075 per cent. The second sample was browny-yellow in colour, and again protein was in gross excess—over 400 mg. per 100 c.cm. The protein content remained at over 400 mg. till the twenty-fourth day, when it dropped to 140 mg., and the C.S.F. was almost clear. At no time were there more than 4 or 5 white cells per c.mm. The report on the final sample taken on the 35th day day was: "Fluid clear; protein 180 mg. per 100 c.cm.; globulin in excess; chlorides 0·7 per cent.; sugar 0·05 per cent.; cells under 1 per c.mm."

At the beginning of her illness the patient was given a mixture containing Hexamine 10 grains thrice daily; but it was discontinued on the fourth day because she disliked it, and it seemed clear that lumbar puncture was the only really useful treatment. She said she felt better after each puncture. On occasion aspirin or a compound phenacetin tablet was given for discomfort, but very little was ever needed. Early in the illness we made sure of the availability of an automatic respirator in case the muscles of respiration should fail, but this was not needed.

When I saw the patient three months after the illness was over she was in excellent health, without symptoms or disabilities.

ACUTE DUODENAL OBSTRUCTION

By K. S. Nigam, M.D. Allahabad, F.R.C.S. Edin., D.T.M.

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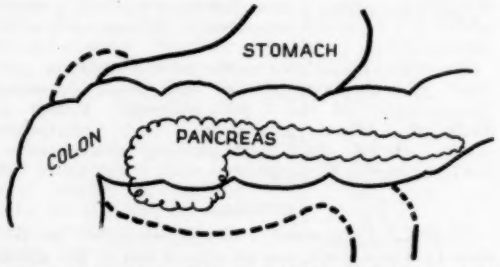
It is an old saying that "the abdomen is a temple of surprises"; and with all the modern methods of clinical investigation at his command there are still occasions when a surgeon making a laparotomy has little idea of what he will find.

A. B., aged 16, Hindu, male, vegetarian, unmarried, was admitted to our surgical wards at about 10 A.M. on Jan. 16th, 1936, complaining of three days' pain in the upper part of abdomen and two days' vomiting. The history was that with no antecedent trouble whatever, on the morning of Jan. 13th he went to defæcate and had a scanty evacuation; he did not strain in the act. Simultaneously he felt a mild colicky pain across the upper half of abdomen, and with frequent exacerbations this persisted throughout the day and the night following. He stayed in bed, stopped all food, and took some carminative mixture. On Jan. 14th and 15th the pain became more frequent and severe. He vomited about six times on the 14th and eight times on the 15th, and in the evening of the 15th he had an enema without result. A particularly restless night followed and he was sent to hospital. The only point of interest in the previous history was that two years ago he had suffered from a similar pain which passed off in a few hours, without vomiting.

Examination.—The patient was thin but wiry; his expression was pinched and anxious. The abdominal walls were receding but moved freely on respiration. The abdominal reflexes were normal and there was no cutaneous hyperæsthesia. The epigastric and right hypochondriac regions were tender to deep pressure. There was no guarding of muscles but the supraumbilical part of right rectus muscle offered greater resistance to palpating hand than elsewhere. During examination an indefinite round mass about 2 in. in diameter was felt a hand's breadth to the right of umbilicus; it was tender, moved with respiration, varied in size, and was tympanitic. Within 10 minutes this lump had disappeared, and no further trace of it could be detected by any manœuvre or manipulation. (It was probably a segment of bowel in spasmodic contraction.) Rectal examination showed nothing abnormal; two high rectal enemas, at an interval of an hour, gave no result beyond return of the fluid. The pulse-rate was 62–68, the temperature 96·0° F., the respiration-rate 24, and the blood pressure 118/64. The urine (spec. gravity 1026) gave a positive test for acetone but not for diacetic acid. The leucocyte count was



Findings at operation. The interrupted line indicates the extent of the hæmorrhagic effusion.

10,000 per c.mm. (80 per cent. polymorphs and 20 per cent. lymphocyte); no abnormality in the number or size of red blood corpuscles was detected.

Treatment.—In view of acetonuria, vomiting, and lack of proper nursing from the start of illness, expectant treatment was adopted with Fowler's position, administration of 5 per cent. glucose in saline by proctoclysis as well as intravenous drip, and turpentine stupes to the abdomen. In the afternoon the patient had two more severe attacks of colic and vomited twice; he passed no fæces or flatus, and the abdomen was slightly distended in the middle. His pulse-rate rose to 116 and his temperature to 101° F. On a provisional diagnosis of acute high intestinal obstruction laparotomy was performed at 6 P.M. on Jan. 16th.

Operation.—Entry through right paramedian umbilical incision. Collapsed jejunum and ileum encountered. No free fluid in peritoneal cavity. A transversely elongated oval purplish-black mass was found under the transverse colon which was held up with empty stomach and liver pushed above under the ribs. This mass was tympanitic. The peritoneum on this mass below the transverse colon was incised, and 8–10 oz. of tarry blood escaped. On mopping this away normal pancreas and duodenum were exposed and thoroughly examined by incising the peritoneum widely; but no abnormality such as a true cyst of the pancreas, diverticula, or ulcers of the duodenum was detected. There was no active bleeding. Simultaneously the jejunum assumed a filled-up appearance demonstrating that the effused blood had caused mechanical obstruction of the duodenum. The superior mesenteric vessels or their branches were not pressing on the duodenum. The hæmorrhagic effusion was found to extend proximally to near the pylorus and distally to about an inch beyond duodenojejunal flexure. The abdomen was closed in the usual way after bringing out a drain of rubber tissue through a stab-wound in the right loin across the right renal pouch of Morrison. Recovery was uneventful, the drain being removed in 24 hours.

Special investigation.—On the 16th, after the operation, the bleeding-time proved to be 3 mins. 45 secs.; next day it was 3 mins. 40 secs. The diastase content of the urine, estimated in the pathology department of King George's Medical College, was 20 units per c.cm, (Jan. 17th), and the pathologist, examining tissue, &c. removed at operation, described them as "blood-clot covered with endothelial cells which are probably derived from the peritoneum—a peritoneal blood cyst." Clot culture from the contents of the cyst was sterile after 24 hours' incubation. No microfilariæ were detected in the night blood. Loewi's test was negative. Acetone disappeared from the urine on Jan. 20th. Opaque-meal skiagraphy on Feb. 7th by Dr. Raghunandan Lal showed a J-shaped type of stomach with no indication of ptosis, niche, or accessory pocket. A certain amount of gastric residue was present after 1½ hours. The meal passed rapidly through the first and

second parts of duodenum, but was held up again in the third part of duodenum. No evidence of ulcer.

In this case there is no history of trauma except that the pain started during defæcation, which may imply some straining, though the patient denies it. If he did strain why did hæmorrhage occur round the duodenum? No hæmorrhagic diathesis was indicated, and the bleeding-time was normal (platelet count not done). The head and body of pancreas were carefully exposed, but no abnormality was found; there was no fat necrosis or sign of pancreatic insufficiency or irritation. No gastro-duodenal ulcer was found at the operation or was indicated by skiagraphy. The cause of the illness thus remains undetermined. The patient is at present in excellent health.

MEDICAL SOCIETIES

WEST LONDON MEDICO-CHIRURGICAL SOCIETY

THIS society met on Jan. 8th at the Vere Hotel with the president, Mr. NEIL SINCLAIR, in the chair, and Mr. ERIC PEARCE GOULD, president of the Medical Defence Union, opened a discussion on the

Defence of Negligence Actions

A patient had a right, he said, to expect that his doctor would exercise reasonable skill and care; the failure to do so was negligence. Complaints of medical negligence were increasing, for various reasons. The old-time mutual confidence between doctor and patient was unfortunately lessening; lay people knew more about medical matters, particularly about X rays; there was a certain news value in the doctor's peccadilloes, and the publication of accounts of actions against doctors encouraged others to complain. The gravity of negligence actions was also increasing, partly because juries tended nowadays to award very high damages, and partly because recent legislation had extended liability for the results of negligence beyond the person of the doctor to his estate after his death. An action could be brought against a firm of partners for the negligence of one member, and it was therefore essential that each member should belong to a defence society, and convenient that all should belong to the same society.

Negligence actions, he continued, fell into four groups, the first of which comprised actions brought out of pure malice, to avoid the payment of fees. A summons served by the defence society would often bring payment, sometimes outside the court immediately before the hearing. Secondly, when the act was really negligent, a settlement must be made on the best terms at the earliest possible moment. Third came the actions in which there was prima facie evidence of negligence but, from a medical point of view, a good defence. If the plaintiff were reasonable it might be wiser to settle, or to deny negligence, prepare the defence, await a moment when the patient's demands were not quite as exacting as they had been, and then settle; the defence might, on the other hand, be good enough to take into court with a fair chance of success. One cause of such actions was the transfer of a patient from one doctor to another in the middle of a course of treatment—e.g., a plaster splint for a fracture—planned by the first doctor; when it failed, the patient might blame the second doctor without good cause. Sometimes the society considered the defence to be excellent but the doctor feared that even a successful result would injure his practice; the society would then try to meet his wishes.

The fourth and last group consisted of cases in which negligence had clearly been committed but the doctor was not to blame, a class which seemed to be multiplying. Until a generation ago it had been generally accepted by the profession that the doctor was responsible for all that happened in a case, and not so very long ago the protection societies had succeeded in establishing for practical purposes the principle that an anæsthetist was responsible for his own errors and had exonerated the surgeon from liability for injury in matters within the anæsthetist's particular province. The time might have come for recognising the responsibility of other assistants. Modern medical work increasingly needed the coöperation of a team of workers, each trained in his or her own particular duties. It was right and proper that such duties should be delegated to the carefully trained assistants of to-day. While no surgeon could be exonerated from seeing that the members of his theatre team were properly trained, most medical men would feel that if he did this, he was then entitled to rely upon his assistants for seeing that the swabs and instruments were correctly counted. A South African appeal court (Van Wyk *v.* Lewis, 1924, S.A.L.R. 438) had given a ruling exonerating the surgeon in a case where a swab had been left in after the theatre sister had reported correct. A surgeon ought also to be entitled to rely upon the ward sister not to burn the patient with hot-water bottles after he returned to the ward, or to remove in due course drainage-tubes inserted at the operation. A surgeon should not carry quixotry so far as to take the blame for a nurse's negligence merely because her shoulders were weaker than his.

In conclusion, Mr. Pearce Gould suggested that all doctors ought to realise the many pitfalls of medical practice and be increasingly careful. A doctor who felt conscience-striken should not commit the error of telling the patient how blameworthy he considered himself. A doctor should never criticise before the patient or his friends the treatment of another doctor, and, most important, every practising doctor should belong to a medical defence society and pay his subscription regularly; 20 per cent of members were late every year in paying their subscriptions and therefore fell out of benefit for a time. A doctor faced with a complaint of negligence should consult his society at once, and the first reply to any communication he received should be dictated by their experience rather than by his feelings of the moment. Finally, having consulted his society, the doctor should do what he was told.

Mr. C. T. LE QUESNE, K.C., said that the possible defences to an action for medical negligence were, first, that there had been negligence but the doctor had not committed it, as when a pair of forceps had been left in a patient's body at a previous operation (Crotch *v.* Miles [1]). Secondly, the doctor might plead that, although the patient was not satisfied, he had taken reasonable care and used reasonable skill and had therefore not been negligent; this defence particularly applied in cases where the

[1] *Lancet*, 1930, 1, 643, 706.

medical evidence conflicted. Thirdly, he might plead that he was not responsible for the negligence of another person. The court would always have to hear the evidence, including evidence of the custom governing the particular operation or treatment, and decide whether in all the circumstances the responsibility rested with the doctor or with one of his assistants.

DISCUSSION

Mr. W. McADAM ECCLES said that many cases were prevented from coming into court by the good offices of the defence societies. Nursing coöperations varied in the steps which they took to insure their nurses. Some, whose nurses were legally their servants, insured themselves against third party risks. He asked who was responsible when a coöperation lent a nurse to a hospital for service in one of its private wards: the practitioner who gave her orders, the hospital, the coöperation, or the nurse? Other coöperations, besides insuring themselves, insisted that each nurse should take out an insurance policy. The routine of an operation became so much of a habit that it was easy for the surgeon to detect negligence in its performance by any member of the team. He himself never left a nursing-home or house without making sure that there was nothing in the patient's bed likely to do damage. If a doctor was called to give evidence against a colleague he must not hesitate to tell the truth, as he was bound to do by his duty to his profession, the State, and the law.

Mr. G. B. WOODD-WALKER said that the surgeon was peculiarly open to complaints of negligence in his treatment of fractures. The out-patient surgeon, treating a patient who was dissatisfied with the treatment of his general practitioner, often found great difficulty in communicating with the doctor without the patient's knowledge. It was very important that the hospital surgeon should stand by the private practitioner and not allow the patient to have access to records and films which might possibly support a charge of negligence.

Dr. REGINALD PERKINS asked whether a doctor could be charged with negligence for leaving with the patient enough tablets of a hypnotic drug to enable him to commit suicide.

Prof. V. B. GREEN-ARMYTAGE related that a married woman, a deaf mute, whose husband was also a deaf mute, had been admitted to his hospital desiring ligation of her Fallopian tubes on eugenic grounds; her husband joined in the request. The hospital governors had forbidden the operation, taking the view that it would constitute the criminal offence of maiming. Another hospital, however, had admitted her and had allowed an honorary surgeon to perform the operation, to the great and permanent satisfaction of the couple. On another occasion he had sterilised, with the consent of her husband, a woman who had spent six months in Bethlem Royal Hospital with puerperal mania. The man had later threatened an action or prosecution but had been dissuaded by the defence society. Prof. Green-Armytage expressed fear that he had offended against the law or against the husband's legal rights, but mentioned that he had safeguarded himself by performing only a temporary sterilisation—burial of the fimbriated ends in the broad ligament—which could be undone at any time.

Mr. D. HARCOURT KITCHIN said that there was little authority in this country governing the vicarious liability of a surgeon. Perionowsky *v.* Freeman (1866, 4 F. and F. 977) seemed to lay down that the surgeon could not be held responsible if a nurse carried out his orders negligently in circumstances in which he could not supervise or control her actions, when the duty was one which he could properly delegate to her. In the case of Van Wyk the court had found the practice of delegating the counting of swabs to the sister to be reasonable, that she was an independent assistant, and that the surgeon was entitled to rely on her count. Even that judgment had not, however, exonerated the surgeon for every negligent act of one of the team, and it could only be applied to the particular circumstances of that case. In Ingram *v.* Fitzgerald [1] the New Zealand Court of Appeal had decided that the surgeon was not responsible for the mistake of a nurse in painting the patient's body with iodised phenol instead of tincture of iodine. Such decisions merely laid down the principle that in certain circumstances a surgeon might not be responsible for the negligence of an assistant; they did not do more. He asked Mr. Pearce Gould what measure of immunity the profession demanded. He could not imagine Parliament passing an Act exonerating all surgeons from liability for all negligence of a member of the theatre team, nor any decision of the House of Lords which would extend beyond the facts of the particular case. It seemed probable that the surgeon would always be open to actions for vicarious negligence, and that his legal position would be gradually improved as successive decisions exonerated him in particular sets of circumstances. The liability of a coöperation for the negligence of one of its nurses must, Mr. Kitchin thought, depend upon the contracts which the patient had made with the hospital, the hospital had made with the coöperation, and the coöperation had made with its nurse. In Hall *v.* Lees (1904, 2 K.B. 602), where a patient sued a coöperation because one of its nurses had burnt her with a hot-water bottle, the court had found that the coöperation had only undertaken to supply a competent nurse, and not to nurse the patient through her agency. The answer to Mr. McAdam Eccles's question would therefore probably be that the nurse was in any case liable; the coöperation was not liable if it only undertook to supply a competent nurse; the hospital was not liable because she was presumably doing skilled work which its governors could not supervise or control; and the practitioner was not liable for the same reason. He still maintained that the provision of the Law Reform Act, 1934, which gave an aggrieved patient a right of action against a doctor's estate, was not likely to be quite so disastrous as had been represented, because the estate could not claim damages for loss due to the death itself. He could not see what right of action a widow could have against a doctor who entrusted her husband with a lethal number of medinal tablets, for she could not claim for loss due to the death, and the patient could not have claimed damages for injury caused by his own act. He did not know of any enactment or provision of law which would make a gynæcologist liable to a criminal prosecution for sterilising a woman on medical or eugenic grounds, for the old offence of maiming had consisted only in impairing the efficiency of a man as a soldier. A sterilising operation performed without the consent of the woman of course gave her a right of action for assault, as would any other operation.

The PRESIDENT mentioned that he had himself been sued for damages caused by a nurse with a

[1] *Brit. med. J.* 1937, 1, 46.

hot-water bottle, but the Lord Chief Justice had directed the jury that he had no case to answer. His practice had not suffered but had increased after this success.

Dr. H. H. SANGUINETTI asked what investigations a doctor might reasonably be expected to perform in deciding whether an operation was necessary, and suggested that in many cases a white cell count should be made.

Mr. HOWARD STRATFORD asked how a doctor should protect himself against an action for not ordering a radiological investigation when the patient had refused to have one.

Dr. GERALD SLOT said that a prolific source of complaints against physicians was notification of infectious disease. Many deaths attributed to the anæsthetic were really due to prolonged manipulation. Checks against wrong dispensing were in many nursing-homes not carried out as carefully as they might be.

REPLY

Mr. PEARCE GOULD deprecated the use of bankers' orders by members of defence societies, for the member might change his bank and forget to make a new order, and they were harder for the office staff to check. He considered that individual insurance by nurses would lead to many actions being brought which otherwise would not be heard of. Hospitals should take steps to prevent patients having access to the notes of their cases. In every case in which the doctor considered a skiagram should be taken and the patient refused, he should at once put his opinion into writing, either by sending a letter to the patient and keeping a copy or by making a note at the time in his own records. The doctor must always do what he thought best for his patient, regardless of the possibility of legal complaint. The Law Reform Act, 1934, was a serious danger to the relatives of deceased doctors, and both defence societies now undertook to defend an action brought against the estate of a late member.

MEDICAL OFFICERS OF SCHOOLS ASSOCIATION

AT a meeting of this association on Jan. 8th Dr. JOHN LAMBERT (Wellington), the president, took the chair, and Dr. E. KAYE LE FLEMING opened a discussion on the

Education of the Body in Public, Secondary, and Preparatory Schools

The first question likely to be raised, he said, was that of nutrition. In schools of these three kinds it was improbable that the food would be insufficient in quantity; but even the best diet sheets failed to disclose its quality and the way in which it was cooked and served. Unfortunately there were still schools at which fresh fruit was an extra and had to be paid for. Growing boys needed a lot of sugar, and one explanation of the popularity of the tuck-shop was that boys were conscious of the sugar deficiency of their ordinary diet. Spacing of meals was also of prime importance; yet he knew one large public school at which, after their 1 o'clock meal, the boys played Rugby football, had a shower bath, changed, re-entered school, took their work, and got nothing to eat until 6—which he regarded as monstrous. As for fresh air, its full value would probably not be recognised, even in the medical profession, without experience of life in a sanatorium. The ordinary school curriculum did not allow enough margin for this, and there was still a great deal of unhealthy overcrowding in schools where there were dormitories and each boy did not (as at Eton and Harrow) have a room to himself. The main infections in school life were droplet infections, spread by coughing and sneezing, and in one school with a high sickness-rate insistence upon three feet between beds had led to great improvement. As to clothing, most people wore too much, though he must make a large exception for the many girls and young women who had adopted a minimum of clothing, to their great physical advantage. Impact of air on the skin was a real healthy stimulant.

The body, regarded as a machine controlled by the will, was capable of an almost infinite variety of development, especially during the plastic school age. But the object of physical training in schools was not to turn out contortionists or figure-skaters, but to produce a muscularly balanced body, capable of much purposeful energy with a minimum of fatigue; or as the report of the British Medical Association said, a balance of body, mind, and soul. This balance was well seen in birds in flight, slow-motion pictures of which were very instructive. The first step towards getting the new ideas on physical education incorporated into school life was to induce head masters to believe in its value; at present, generally speaking, they were insufficiently convinced. Who should educate the educators? The interesting attempts now being made to ascertain how much a boy will learn in a given time devoted to mental education, compared with what he can learn if part of this time is devoted to physical instruction, promised valuable results. Head masters would say, and with justification, that until parents wanted physical training it would be difficult for masters to supply it. The fact was that the school doctor must educate his head master, and the head master must educate the parents. Opposed as Britishers were to dictators, two dictators yet held sway: the head master and the coroner.

Another difficulty concerned the relation of physical education to games. The two should be linked together; they could not be carried out under two masters, for these would probably be at loggerheads. Perhaps the greatest difficulty of all was to find the right teachers. Who was there who could go into boys' schools and teach physical education on modern lines? Where could such teachers be trained? The answer was, practically, "Nowhere in the country." It was very different in regard to girls' schools. It was a dreadful thing to confess that the remedy was to take a course in Sweden. All through the B.M.A. report on the subject it was made clear that physical education needed close coöperation between teachers and doctors, since the medical was the most important side. But the doctor had almost no opportunity of getting acquainted with physical education, though this was a very important part of preventive medicine. Science had been defined as measurement, yet there was no adequate measure or standard of physical fitness. In the simple matter of heart tolerance to exercise, each medical man had his own standard and method of test, which though of value to himself was of no value to others. It was to the universities one looked for help in this matter, but so far in vain.

The PRESIDENT said that for many years there had been four or five large schools for training teachers of physical education in girls' schools, whereas for men he knew of only the Leeds Training College.

Dr. C. WATNEY ROE (St. Paul's) said the training contemplated was far more important than mere physical jerks. As to diet, though no one in England could be said to be starving, there was a striking absence of calcium, iron, and essential vitamins in many diets. The work of Dr. G. E. Friend, at Christ's Hospital, showed excellent results achieved at a school by a generous and well-balanced diet.—Dr. ARTHUR DAVIES mentioned the work of the College of Hygiene and Physical Training at Dunfermline and Edinburgh. It was extraordinary, he said, that physical education should have been so much ignored by the universities.—Mr. CROCKER contended that only those able to have unlimited fresh air could keep their bodies fit.—Dr. A. H. MACDONALD (Dr. Barnardo's Homes) said that, for teaching physical exercises, his institution had secured a very good type of man from Aldershot, and they were very successful with the children.

Dr. L. R. LEMPRIERE (Haileybury) said he believed that most of the infections at school did not take place in crowded dormitories at night, but in the house and classrooms during the day. It would be a boon if someone would give a handsome contribution to found physical training centres at universities. He agreed that until head masters and assistant masters were thoroughly interested in this matter, advocates would be simply marking time. His only criticism of the B.M.A. report was the demand that three periods per week should be spent by all youths on this subject; that was asking too much, and was unlikely to be accepted.—Mr. TURNER advocated a compulsory half-hour of sleep or rest in the day.

Dr. ELWIN NASH spoke of the importance of having a proper system of heating in schools. He asked whether any figures were available to show the effect of shortening the periods of instruction, comparable with those issued by the Industrial Fatigue Research Board. He meant a break in the morning for cocoa and in the afternoon for tea. He remarked that he had never met a physical training teacher who had made the boys understand the why and wherefore of what they were required to do.—Dr. C. K. ATTLEE held that the physique of girls was now much better than that of boys.—Dr. E. B. MORLEY said he had often asked himself what was the aim of all this physical fitness; what was the boy making himself fit for? The average boy did not look beyond his ability to play games. Was he not, in many cases, making himself fit to endure sitting on a stool in a close office many hours a day? Or sitting in the ill-ventilated law courts listening to endless arguments? In arriving at the proportion of men unfit for the Army at the outbreak of the late war it must be remembered that much of the examining was done by old doctors who considered the presence of a heart murmur meant absolute incapacity and rejection. Not only was it necessary to have regard to what boys were being made fit for, but every effort should be made to render occupations healthy.

HEALTH CENTRE AT BLACKPOOL.—The site of the old Victoria Hospital is being acquired for £30,000 by the Blackpool health committee for use as the health centre of the borough.

LUCY BALDWIN MATERNITY HOME, STOURPORT.—On Jan. 5th Mr. Baldwin opened further extensions to this maternity home which was the gift of Sir Julien Cahn to Mrs. Baldwin who presented it to the Worcestershire county council. Sir Julien Cahn has also met the cost of these extensions.

ROYAL SOCIETY OF MEDICINE

SECTION OF THERAPEUTICS

AT a meeting of this section on Jan. 12th, with Dr. DOROTHY HARE, the president, in the chair, a paper on

Protamine Insulin

was read by Dr. H. C. HAGEDORN (Copenhagen). He began by speaking of the change brought about by the introduction of insulin. At first, he said, its success was so great that nobody thought of improving the remedy, but an improved technique had been found desirable in the severer cases with considerable oscillations in blood-sugar, which needed careful and frequent examinations. The oscillations could be modified by appropriate distribution of the diet and also by better timing of the insulin effect through modifications in the insulin preparations themselves. This second method had been thought of as early as 1923, and his institute had taken much interest in it ever since. Three ways of retarding the effect of the insulin had been tried: first, the emulsification of insulin solution or the suspension of dry insulin in oil, which had not seemed applicable in every case; secondly, the injection of a vasoconstrictor with the insulin; thirdly, the injection of the insulin as a more or less insoluble compound. The rate of absorption of both soluble and insoluble preparations depended on the concentration and on the volume. The insoluble compound differed from the soluble in that the dose could be varied without altering the volume or the concentration in the liquid phase; theoretically an injection of a suspension of an insoluble compound gave a constant rate of absorption until all the particles were dissolved. He had restricted his experiments to those substances that were destroyed or excreted rapidly, fearing that other compounds would sooner or later cause unpleasant surprises. Some experiments with tannic acid compounds had been abandoned because of local reactions, but protamine insulins had been found to be non-toxic in far greater doses than those to be used in treatment, and had a prolonged action clinically. Many protamines had been tried, and salmiridin (obtained from the rainbow trout) had been chosen as suitable. Researches by Mr. Krayenbuhl into the physical chemistry of protamine insulin compounds had thrown light on the effect of mixing doses of the soluble and insoluble preparations. If solutions of protamine and insulin were mixed in varying proportions one proportion was found to which the further addition of either substance (after the production of the first precipitate) would cause the same amount of further precipitation. This proportion, called the isophane proportion, was peculiar in that the ratio of insulin to protamine was the same in the precipitate and the solution. The isophane proportion was altered by the presence of small quantities of zinc which also prolonged the action of protamine insulin. The amount of zinc used in practice was so small that it was generally considered harmless, but the speaker himself only used it for those for whom the protamine insulin alone was not satisfactory. The precipitated protamine insulin was stable for many weeks under ordinary conditions and for months in cold storage. Dr. Hagedorn said that objections had been raised to the name protamine insulinate, because the ending "ate" implied that insulin was an acid radicle. In view of the very complicated chemical nature of the

substance he had dropped the ending and now spoke of protamine insulin.

Caution had prompted him to treat only a few cases with the new material for the first year. Dr. N. B. Krarup had tried the substance in hospital under controlled conditions, carefully observing the blood-sugar, glycosuria, and acidosis. Graphs taken from these results showed the relatively quick action of the soluble insulin and the more even action of the insoluble. The protamine insulin had been used in one daily dose, and he thought that all who regarded protamine as harmless would agree that the compound should be used as soon as it was apparent that one daily dose of plain insulin was insufficient. Protamine insulin was suitable for evening doses, but its effect stopped abruptly, and sometimes the evening dose had to be postponed for this reason. Ordinary insulin might be better suited to the requirements of daytime; in some cases, especially in children, a second dose of the insoluble preparation was useful. The combined use at one time of both types was being tried, both in combined and separate injections. Patients having protamine insulin said they felt better and less tired, and that they had ample warning of hypoglycæmic symptoms, which also tended to last longer. Surgical cases had been easier to deal with, and Graves's disease occurring in three diabetics had improved astonishingly. Many patients who used to be brought to hospital frequently in hypoglycæmic or semi-comatose states had kept out of hospital. Treatment, however, was not successful in every case, for some did not react typically.

Dr. O. LEYTON referred to the leading part taken by Dr. Hagedorn in the evolution of insulin therapy and the boon he had conferred on diabetics by supplying a compound which for many converted a life of hazard into one of comparative monotony. Those who had much experience of protamine insulin confirmed Dr. Hagedorn's results but some might be unlucky with their first cases. In over half of his own cases the prolonged action of protamine insulin had prevented severe hypoglycæmic attacks and also the rise of the blood-sugar in the early morning. It had enabled him to give only two doses a day to some patients who, in spite of much juggling with food, had required three or even four doses of insulin hydrochloride a day. Single doses of protamine insulin given first thing on waking had kept the blood-sugar level to between 0·08 and 0·15 per cent. for twenty-four hours; occasionally this had been astonishingly successful even when a single dose of more than 40 units had been required. Naturally the distribution of carbohydrate had to be adjusted: about 35 per cent. had been given at breakfast, two hours after the injection, and 50, 10, and 5 per cent. respectively at lunch, tea, and the evening meal. The total carbohydrate was often well over 200 grammes. In some, however, hypoglycæmia developed at about 11 A.M., and in others the insulin was ineffective. The variable action of protamine insulin probably depended partly on the site of injection, but a few observations of the effect of intravenous, intramuscular, hypodermic injections and those into adipose tissue had not accounted for the variation. Dr. Leyton thought that if a patient's condition was well controlled upon two doses of insulin hydrochloride a day, not exceeding 12 units in all, no change should be made unless for some special reason he could not give himself or be given an evening dose. For those who were improving and no longer needed 12 units in two doses a single dose of protamine insulin was advisable.

Dr. W. W. PAYNE said that one girl who had been under his care for a long time at the Hospital for Sick Children, Great Ormond-street, had changed conspicuously since being put on protamine insulin. She had been a severe case and very nervous, but now stood up to the accidents of life in a much better way. Although it was still hard to keep diabetic children sugar-free, and although the change to protamine insulin wrought no obvious improvement in physical condition when this was already good, the patients themselves said they felt much better. He had been trying one daily dose on most of his child patients and often found that they remained sugar-free through the night. Unlike Dr. Leyton, he had spread the carbohydrate evenly through the meals. He had had one protamine reaction after using freshly precipitated material and had since avoided preparations which had not been made at least a day before. He asked whether a stronger solution could be made. A dose of 60–70 units occupied nearly 2 c.cm. and was a bulky dose to give to little children.

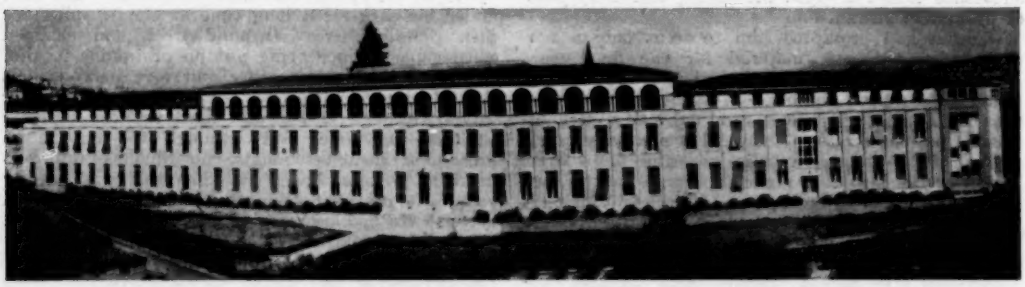
Dr. GEORGE GRAHAM had had some patients suffering from hypoglycæmia after protamine insulin; some of them who had formerly had no warning told him that they could now tell when an attack was imminent. He thought the new treatment would be very useful for patients with big variations in blood-sugar. He wished there were a third type of insulin, quicker in action than the hydrochloride.

Dr. T. IZOD BENNETT had been able to reduce the total amount of insulin his patients were receiving although they were having only one injection a day. He had been able to abolish the hypoglycæmia which had commonly developed before breakfast. The change in temperament noted in his patients since using protamine insulin had shown him how much the fear of hypoglycæmia had haunted them before and how it had been a cause of nervous irritability. He thought the introduction of new forms of insulin was going to make the physician's work much harder. He avoided the use of two kinds of insulin in one patient, for he felt that if a patient had two kinds to give himself accidents were bound to happen sooner or later. Slow insulin had come to stay, but he hoped doctors would not use two kinds at once. He expressed regret that the protamine insulin should all come from abroad and that the British manufacturers always walked in the rear of other countries.

Mr. F. H. CARR, D.Sc., speaking on behalf of the manufacturers, said in reply that the British firms were collaborating in the production, but had delayed putting protamine insulin on the market, at Dr. Hagedorn's request, until a uniform and well-tried product could be issued. There was a patent on the preparation which, except by the courtesy of Dr. Hagedorn or by contravention of the patent, prevented them from making it.

Dr. HAGEDORN thought a stronger solution of protamine insulin might be made, but he was not sure that its action would be so prolonged. A single daily dose was the ideal, but infection and other causes often made two doses preferable. It had been said that diabetic patients sailed uncharted seas; and he thought the same might be said of their doctors. He wished them a happy voyage.

NEW SURREY HOSPITAL.—The Surrey county council is proposing to erect a large hospital in Carshalton with accommodation for 832 patients to meet the growing needs of the county. The nurses' home will house 340 nurses.



AN ATHENS HOSPITAL

THE Marika Eliadi Maternity Hospital was given to the city of Athens by Madame Helena Venizelos in memory of her friend whose name it bears. It is a three-storeyed building which stands in beautiful gardens looking towards Mount Hymettos. The large square entrance hall is of rose-coloured marble, and from it white marble stairways lead to the first floor where there are wards for patients who pay small fees or none at all. The colour scheme on this floor is pink and white and each room accommodates ten beds and their cots. They are large and well ventilated with big windows looking over the gardens. The more expensive rooms are on the second floor and here the colour scheme is green and gold. Large windows lead from each room to a wide shady verandah that runs the length of this floor. There are three operating theatres, three large labour and delivery wards, consulting-rooms, and an out-patient department where patients may attend three times weekly. The administration rooms, the staff dining-rooms, and the all-electric kitchens are on the ground floor.

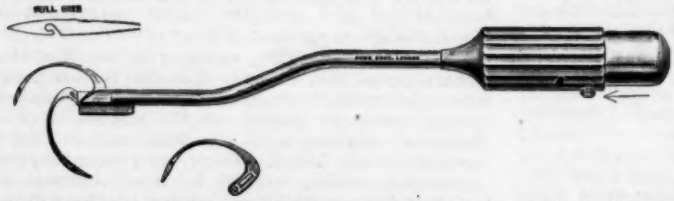
The total number of beds in the hospital is 130, of which 50 are reserved for non-paying patients; there are 80 to 100 cots. About 2000 babies are born yearly, and many gynæcological cases are also treated. Neither money nor trouble has been spared in making the equipment and arrangements as good as they can be made and Madame Venizelos has provided funds to maintain the hospital during its first few years. The head of the medical staff is Prof. N. Louros, who holds the chair of obstetrics at the University of Athens.

A school for midwives, founded by Madame Schilizzi, the mother of Madame Venizelos, is attached to the hospital, and the matron is also superintendent of the school. It accommodates 40 to 50 student midwives, and provides pleasant living quarters for the nursing staff of the hospital. The students receive a three years' training, and on qualification they return to their homes in the provinces to spread the principles of hygiene among the people.

NEW INVENTIONS

IMPROVED NEEDLE-HOLDER FOR PROSTATECTOMY

THE widespread performance and success of Harris's operation for suprapubic removal of the prostate necessitates a periodic review and possible alteration of the armamentarium. Two criticisms of the needle-holder appear to be justified. In the first place,



the fact that the shaft is straight causes the operator's hand to obscure the operative field and to make it difficult to place the catgut in the appointed slot, especially if the operation is complicated by an adipose abdominal wall or narrow pelvis. The second difficulty is that the actual insertion of the needle may induce bleeding. Harris states that "in order to avoid hæmorrhage from the needle puncture, it is important that the needle should not have a terminal sharp cutting edge. The needle should be sharpened only at the actual point. It is made of rustless steel, and must be kept sharp." I do not consider that this precaution goes far enough. The needle commonly supplied with the Harris needle-holder is flattened from side to side, and although there is no cutting edge, a slit-like opening is produced which may induce hæmorrhage when the needle is inserted.

In an attempt to obviate these two difficulties I have designed a needle-holder which has two main characteristics. The shaft is angled about half-way between the needle and the holder. This permits a clear view of the needle both at the moment of insertion and immediately afterwards, by keeping the operator's hand out of the line of vision. The angle involves the pilot being made with a series of joints similar to a chain so as to pass the bend. Secondly, a round-bodied needle is provided. In order to eliminate the occasional annoyance of the catgut slipping out of the slot before being drawn through the tissues, a lateral slot that renders this accident impossible is provided with the round-bodied needle.

I have now used this needle-holder in many cases and have found it very satisfactory. The angled shaft permits a good view of the depth of the wound and the round-bodied needle causes no additional hæmorrhage. Finally, the needle appears to bite readily into relatively tough tissue.

The needle-holder was made for me by Messrs. Down Bros., Ltd., 22A, Cavendish-square, W.1, who also suggested the lateral suture-holding slot.

J. COSBIE ROSS, Ch.M. Liverp., F.R.C.S. Eng.,
Honorary Assistant Surgeon to the Liverpool Royal Infirmary and Demonstrator of Operative Surgery in the University of Liverpool.

REVIEWS AND NOTICES OF BOOKS

Methodik der Hormonforschung

Vol. I. By Dr. Phil. CHRISTIAN BOMSKOV. Leipzig: Georg Thieme. 1937. Pp. 716. RM.56.

THE first volume of this work deals with general laboratory methods and with the hormones of the thyroid, parathyroid, adrenal cortex and medulla, and the pancreas. It is remarkable for the detail in which it describes all the working methods which may be used in the chemical and biological investigation of hormones and, in particular, of their assay. Thus the subjects included in the 142 pages of the "General Part" range from a description of necessary surgical instruments and general operative methods to electrometric measurements of *p*H, whilst the theoretical side is not forgotten, and there are pages on the principles of biological assay and the mathematics of dose-response curves, with a welcome emphasis on the necessity of basing all biological assays on comparison with standard preparations and international units. In the "Special Part" the matter is arranged under the headings of surgical, histological, biological, pharmacological, and chemical methods, and the treatment is so full and inclusive that, whether the subject be the preparation of thyroglobulin or the assay of adrenal cortex extracts, any method of repute is described in sufficient detail for it to be carried out by a competent worker.

It is too often true of a work of this compilatory character that it is uncritical—in some respects it must be, where the subject is controversial, and the author must keep a judicial attitude while the case is still being argued—but here this conclusion would be unjust, for the author has a sufficiently wide first-hand knowledge to be able to indicate clearly and authoritatively the advantages and disadvantages of any method and its sphere of usefulness and limitations. The author intends the book "for chemists and physiological chemists, for the medical man engaged in scientific work, and for the clinician." It does in fact combine chemical and biological information in just the way to be useful to all those laboratory workers in endocrinology who, primarily trained in one or other science, find themselves in this subject working on the frontiers between them. For any type of worker, whether purely scientific or technical, it is a mine of information which can save the labour of many references to the original literature.

A Synopsis of Hygiene

Fifth edition. By W. W. JAMESON, M.A., M.D., F.R.C.P., D.P.H., Professor of Public Health, London University, and Director of Public Health Division, London School of Hygiene and Tropical Medicine; and G. S. PARKINSON, D.S.O., M.R.C.S., D.P.H., Lieut.-Colonel R.A.M.C. (Ret.), Assistant Director, London School of Hygiene. London: J. and A. Churchill Ltd. 1936. Pp. 623. 21*s*.

A FRESH edition of this well-known text-book was called for because of the mass of new public health legislation passed in the present year, and the opportunity has been seized for revising much of the text and bringing the synopsis fully up to date in science as well as in law. The title of this book aptly describes its purport and the positions held by the authors and their collaborators guarantee it as a sound exposition of British public health science, practice, and tradition. The main appeal of the book is to students for the D.P.H. course and to entrants to the various branches of public medical practice, but experienced practitioners may refer to it for details which they are apt to forget. It is designed to give, under each section, as much as every medical officer of health is expected to know and nothing in the non-medical field which he need not know; it does not profess to deal fully with the strictly medical duties of health officers. But it leaves no subject untouched and is a true and full synopsis of preventive medicine.

Despite the condensation of the material the book is agreeable to read and it is remarkably free from errors. Indeed, we have noticed only one mis-statement—namely, "Every five years the M.O.H. must issue a survey report." Survey reports are required only when the Ministry of Health calls for them; the last call was in 1930, none was required for 1935. The index is good; the references at the end of each paragraph are valuable. This is a thoroughly sound and useful book which should find a place in the current library of every public health practitioner.

Textbook of Pathology

Sixth edition. By W. G. MACCALLUM, Professor of Pathology and Bacteriology, Johns Hopkins University, Baltimore. Philadelphia and London: W.B. Saunders Co., Ltd. 1936. Pp. 1277. 42*s*.

THE fact that MacCallum's text-book is enjoying its twentieth anniversary is sufficient proof of its continued usefulness and popularity. Like its predecessors the present edition is arranged on an ætiological classification and not on the conventional system of organ headings. The method has its advantages, particularly in giving the student a better concept of disease as a process and in avoiding any tendency to turn morbid anatomy into a series of "pots." On the other hand it has the disadvantage that in the present state of our knowledge many diseases cannot be so classified and this makes the book less easy for quick reference; the index is however sufficiently good for this disadvantage to be minimal.

Although the general lay-out of the book is the same, there have been numerous additions and alterations; in fact few of its 75 chapters have survived unchanged, whilst several new ones have been added. The additions have filled in the omissions we noted in the last edition and include newly described conditions such as healed pyelonephritis in children, monocytic leukæmia, von Gierk's disease, and granulosa-cell tumour. Naturally the size of the book has increased a little, but with the 66 extra pages the reader gets 45 new illustrations. The new edition can be confidently recommended for its up-to-date information on all branches of pathology. As a work of reference it should be no less useful.

Theory and Practice of Psychiatry

By WILLIAM S. SADLER, M.D. London: Henry Kimpton. 1936. Pp. 1231. 42*s*.

THE author of this enormous book holds, as he says in his preface, that there is a "dearth of practical literature dealing with the non-psychotic groups of mental disorder," and he attributes this dearth to a bias towards an "institutional" conception of psychiatry on the part of those who have written

the accepted text-books. His work is designed to make good the omission and is addressed not only to psychiatrists but to all physicians, sociologists, psychobiologists, and other trained men and women (clergymen, nurses, &c.) who may be desirous of doing something, directly or indirectly, in the fields of preventive and curative psychiatry. The work is divided into five parts. The first deals with general principles and the second with personality problems: these make up a third of the book. The neuroses occupy the twenty-three chapters of Part 3; in Part 4 (134 pages) the psychoses are described, and the last part (244 pages) is devoted to psychotherapy.

Numerous books have been written by psychotherapists for the same reasons as prompted Dr. Sadler. His own book is well intentioned, anything but abstruse, attractive for many people in its emphasis upon the value of religious and similar ideals, and its almost pastoral psychotherapy. It is based on the long experience of its author as director of the Chicago Institute of Research and Diagnosis, a clinic for the treatment of paying patients; it is, moreover, fortified by references to books and articles dealing more authoritatively with some of the topics raised. But the customary faults of such literature are here more than usually conspicuous. It is diffuse, neither learned nor penetrating. Commonplace reflections on the world and human nature are set down—either plain or translated into technical terms—as important psychological principles, while many of the crucial problems of morbid psychology are ignored. Psychiatry as a whole is treated inadequately.

Favourite Prescriptions

By Various Authors. Edited by Sir HUMPHRY ROLLESTON, Bart., G.C.V.O., K.C.B., F.R.C.P.; and ALAN A. MONCRIEFF, M.D., F.R.C.P. London: Eyre and Spottiswoode. 1936. Pp. 227. 10*s.* 6*d.*

WHILST the older generation of physicians deplores the fact that the art of elegant prescribing is moribund, the younger replies that, when a specific remedy is known, there is no need to prescribe a blunderbuss. The general practitioner, whose contact with the sick is more intimate than that of any physician, will probably think that the prescriber is more important than the prescription. Whatever the truth, the compiler of a hospital pharmacopœia has to consider not only simplicity and elegance but also, and above all, economy. This book contains 18 articles originally published in the *Practitioner*. Each of the first 17 discusses the pharmacopœia of one of the great general or special hospitals and is written by a member of its staff. The final article, by Dr. E. Lewis Lilley, gives an account of the National Health Formulary. The reader, who should find herein much to interest and amuse him, may wonder if some of the old remedies which survive do so for any other reason than that they are sentimentally associated with the name of a famous figure in hospital medicine. Incidentally he may wonder who "Uncle Henry" was, this being the name used affectionately by East End patients to connote the uncoated pil. colocynth. c̄ hyosc. B.P. Another point of interest among many is the fact that Guy's Hospital consumes some 2000 gallons yearly of liquid paraffin, whereas St. Mary's makes shift with a mere 330 gallons. It may also be noted that most of the pharmacopœias now include some method of giving iron in massive doses in a compact form so that the patient is no longer compelled to swallow vast numbers of pills daily. The prize for survival among remedies must surely be awarded to salicylic acid. In the Regimen Sanitatis of the eleventh century it is stated that "willow bark treated with hot vinegar dissolves warts." In the form of collod. acid. salicyl. it is still prescribed for the same purpose in the National Formulary. There is a foreword by the senior editor and an index is appended.

The L.C.C. Pharmacopœia

Compiled by a Departmental Committee. London: P. S. King and Son, Ltd. 1936. Pp. 279. 1*s.* 6*d.*

FROM a preface contributed by the medical officer of health we learn that this pharmacopœia is the work of a departmental committee composed of members of the L.C.C. hospital and central medical staff, assisted by eminent authorities on modern medical and pharmaceutical practice. A study of the book soon confirms the expert nature of the production. Two hundred and seven pages are devoted solely to drugs and formulæ. Short notes are given on all the medicinal drugs and preparations of the British Pharmacopœia and the more important ones of the British Pharmaceutical Codex. Unlike most hospital pharmacopœias, the B.P.C. preparations are here given preference to formulæ which differ only in detail from those more widely known. This is an excellent step in the right direction. Drugs and preparations subject to Schedule I and Dangerous Drug restrictions bear distinguishing marks, and this help might well have been extended to drugs in Schedule IV of the Poisons List and Rules. The increasing use of parenteral injections is recognised in the long list of ampoules. Sterilised water for intravenous injections is prepared in accordance with the B.P. 1932. The Addendum has modified its preparation, and it is unfortunate that this and many other changes were not available to the compilers. Prepared ergot, the best preparation now available, is prescribed in capsules of 5 grains; no mixture containing the liquid extract has been included—a step which will be approved by all obstetricians who still prefer ergot to the isolated alkaloids. Somewhat surprising is the absence of any reference to ergometrine. Special L.C.C. formulæ are more numerous in the collection of mixtures. The use of liquid extracts instead of large doses of the corresponding tinctures serves economy without loss of therapeutic activity. A few parochialisms however find their place. Why for instance is mist. magnes. sulph. c̄ senna included as well as the mist. sennæ co. of the B.P.? Ammonium bromide which has lost its official status occurs in two mixtures. Mist. cascaræ co. might have been made more palatable by using the elixir in place of the liquid extract. A syrup or an elixir of ammonium mandelate would have been a welcome addition. Pills have disappeared and a comprehensive list of tablets appears in their stead. Antitoxins, sera, toxins, and vaccines are adequately represented, but there is no reference to staphylococcus antitoxin. The common proprietary arsenobenzene preparations are omitted. Time-honoured tables, such as dentition, incubation and quarantine, methods of administration of drugs, collection of pathological specimens, urine testing, and treatment of acute poisoning are well compiled.

The preface claims that at the time of its publication this pharmacopœia was the most comprehensive and up to date of its kind, and expresses a hope that it may also be found useful by medical practitioners in general. Both the claim and the hope are fully justified; any practitioner would find the book a mine of useful information.

THE LANCET

LONDON: SATURDAY, JANUARY 16, 1937

DRUG COMPOUNDING IN HOSPITALS

THE hospital population under the jurisdiction of the London County Council is a very large one, since that body now controls the institutions which until six years ago were administered by twenty-six separate authorities. Just as one of the objects of the amalgamation of industrial concerns, otherwise known as rationalisation, is economy, so it should be possible to effect a saving in the cost of administration when so many hospitals are brought under the control of a central authority. It may be assumed that the L.C.C. in embarking upon the compilation and publication of a common pharmacopœia for all the institutions which it administers was actuated by the dual motives of securing uniformity of practice and economy in the drug bill, and a careful examination of the book (reviewed on p. 152) suggests that in the endeavour to keep the costs of the pharmaceutical departments within bounds there has been a careful avoidance of any attempt to be economical at the expense of efficiency. Nor is there any desire on the part of the central authority that medical officers should be restricted to the formulas which appear in the new book; thus it is expressly stated in the preface that there is no intention to interfere with the freedom of the medical staff to prescribe what they consider necessary or desirable.

A question which naturally occurs to the mind is whether the publication of a pharmacopœia for the use of all the hospitals under the jurisdiction of the L.C.C. may be taken as a token that at some future time a central manufacturing laboratory may be established for the purpose of supplying all the units not only with approved formulas but also with compounded drugs. As is commonly known, a central buying department for the L.C.C. institutions has been in existence for some time and it may be that the idea, or the practicability, of an extension of the principle of central buying to central production is in the minds of some members of the council. It may be recalled that a scheme for a coöperative arrangement between the London voluntary hospitals was advocated some years ago; for some reason, however, it did not reach the stage of activity which its promoters had desired. But whatever the future plans of the L.C.C. may be, the publication of their pharmacopœia is a commendable undertaking. It is a practical book, containing abundant evidence of having been prepared by practical men and, being the latest hospital pharmacopœia, it should give valuable hints to those whose duty it is from time to time to revise other pharmacopœias. Excellent material for such a revision is provided in the annotated collection of hospital pharmacopœias just issued under the hand of Sir HUMPHRY ROLLESTON and Dr. MONCRIEFF (see p. 152). Very wisely the compilers of the L.C.C. volume have employed the British Pharmacopœia and the British Pharmaceutical Codex as a basis for their work. Unfortunately the book was in the press when the Addendum 1936 was published so that no recourse was possible to the formulas and amended monographs in it; that, however, is a matter which can, and indeed should, be corrected by a short supplement.

The recognition in these volumes of the vital importance of drug compounding makes it all the more desirable to bring the nomenclature of the pharmaceutical branch of hospital practice into conformity with modern usage; the "dispensary" in future should be known as the pharmaceutical department and the "dispensing chemist" as the pharmacist. At last week's meeting of the council of the Pharmaceutical Society it was officially stated that the Post Office had, on representation being made to it, agreed to discontinue the use of the term "dispenser" or "dispensing chemist" for certain appointments and to substitute the description pharmacist. At the same meeting the secretary of the Society was instructed to communicate with the British Hospitals Association in respect of the voluntary hospitals, and with the Ministry of Health in respect of institutions under the control of local authorities, with a view to the adoption of the same policy. "Pharmacist" is a statutory title, and there seems to be no reason why it should not be uniformly employed.

SURVIVAL AFTER RADIUM

IN their seventh annual report, published this week, the National Radium Trust and Radium Commission include an analysis of results obtained at their associated hospitals in the treatment of cancer at certain sites. The first fact to be noted about the figures is that the proportion of patients who die from unknown causes is rapidly falling, and few are nowadays lost sight of—only 3·9 per cent. of those who came for treatment in the years 1930-32. As Dr. BRADFORD HILL points out in his article this week on medical statistics, completeness of this kind is vitally necessary for accurate assessment of the results of any form of treatment, and it is encouraging to note the importance here attached to the energetic work of the follow-up departments. The period covered by the report is 1930–32, and the records of 5600 patients are analysed. The sites studied are five (breast, cervix, lip, tongue, and floor of the mouth) and the customary test of success is applied—namely, the survival-rate or, as it is here termed, the net survival-rate, defined as

"the proportion of patients who are alive, irrespective of the presence or absence of active disease, to the total number of patients treated, including those who have died of operation, but deducting from the total number patients dead from other causes than cancer and patients lost sight of."

In addition a new measure has been introduced, termed the "symptom-free rate," and denoting the proportion of patients who have remained free from symptoms for a given period after the begin-

ning of treatment. The argument in favour of this rate is that it may enable the success or failure of a method to be judged sooner than can be done when the survival-rate is used. For instance, with experience it might be possible from the trend of the symptom-free rate in the three-year period to estimate the survival-rate at the end of five years. At present the volume of material does not suffice for such a purpose, nor indeed to show whether the two rates are in fact more highly correlated than the two survival-rates at the same points of time.

In reviewing so detailed an inquiry we can attempt only brief and selective reference to the results. It appears that 70 per cent. of the women with carcinoma of the breast who presented themselves for treatment in Stage I of the disease survived three years, and 50 per cent. five years. Of those in Stage III, on the other hand, only 18·8 and 13·6 per cent. were alive, many of these being given only palliative treatment. The 2058 patients with carcinoma of the cervix were divided into four stages: of those in the earliest group 61·1 per cent. survived three years and 49·4 per cent. five years, whereas of those in the latest group only 12·6 per cent. were alive after three years and 7·2 per cent. after five. Figures for carcinoma of the lip show, as might be expected, the great importance of involvement of the glands. Of those in whom the growth was limited to the lip slightly more than three-quarters lived five years; of those with the regional lymph glands affected less than a third survived as long. Whatever the stage of disease, the outlook with carcinoma of the tongue is depressing, for of the patients most favourably placed only a quarter are alive at the end of five years, while out of 30 advanced cases only 1 remained. The floor of the mouth gives less unsatisfactory results than this—at least when the glands are not involved—for rather more than half the patients lived five years. With each of these sites, as has been shown over and over again, the chances of survival are better, often much better, if local spread or metastasis has not taken place. Yet the report shows that the proportion of patients in whom the disease is still localised to its original site when application for treatment is made, amounts, for all the sites investigated, to only 25 per cent. This figure varied but little between 1930 and 1932, although there was reason to think that the proportion coming for radium treatment at an early stage was increasing slowly among those with carcinoma of the lip, tongue, and cervix uteri. Younger patients with the latter or with carcinoma of the breast to some extent tend to seek treatment at an earlier stage then those who are older. The question of age is also studied in relation to survival, in two groups, under and over fifty years. For carcinoma of the breast there is no significant difference though the figures suggest a slightly more favourable issue in Stages I and II with the older patients. For the cervix this difference is definite and gives statistical support to the belief held by many clinicians that the prognosis is rather worse in young patients. For the remaining sites the data are insufficient for investigation of any relationship between age and survival. For these, too, any study of the relative success of different methods of treatment has had to be postponed till more material has accumulated, though those that prevail have been tabulated. One very serious obstacle to such a study is the large number of different combinations of methods of treatment. For instance 86 such combinations were distinguished in treatment for carcinoma of the breast, 66 for the cervix, 56 for the lip, 110 for the tongue, and 53 for the floor of the mouth. Some attempts to cope with this problem have been made for the breast and the cervix. Patients with carcinoma of the breast in Stages II and III show a slightly better three-year survival-rate and a higher symptom-free rate when treated by interstitial irradiation combined with excision than when treated with interstitial irradiation alone, but with the smaller number of patients observed for five years there seems to be no clear advantage of one treatment over the other. For carcinoma of the cervix there is a suggestion that the use of X rays combined with the Stockholm method of treatment gives a greater freedom from recurrence than the Stockholm method alone; but the survival-rates at three years under the two methods show no material difference.

In judging these various and numerous survival-rates it must be remembered, as the report emphasises, that they give a picture of the average results of radium treatment at a very widely scattered group of hospitals, and "must not be compared lightly either with the results of special clinics, or with results based upon a picked series of cases treated by a highly skilled surgeon. On the contrary, the results . . . may be said to be those achieved by the medical skill of a large part of the country working with radium, in conjunction with other methods, upon the average cancer patient seeking treatment." The statistical treatment of the data and their presentation have, we may add, been carried out with obvious care and skill.

CARBON MONOXIDE POISONING

So long as coal gas is used for heat and illumination, carbon monoxide poisoning will be of great interest and importance. Dr. HARVEY G. BECK [1] of Baltimore says that in New York only highway accidents exceed it as a cause of death. We are familiar now with the way in which carbon monoxide, with its high affinity for hæmoglobin, displaces oxygen from the blood and produces a fatal anoxæmia without the usual symptoms of asphyxia. Symptoms may be absent altogether, or present only as a kind of mental confusion, according to the concentration of the gas and activity of the victim. This feature is at once the attraction to suicides and the trap to the accidentally exposed. The struggle for air and extreme distress that we associate with suffocation are due to accumulation of carbon dioxide in the alveoli of the lungs, and there is no such accumulation in carbon monoxide poisoning. Indeed the

[1] *J. Amer. med. Ass.* Sept. 26th, 1936, p. 1025.

hyperpnœa that may accompany this—though almost ineffective and perhaps unnoticed at the time—actually lowers the carbon dioxide content of the blood, leading to a state of affairs which many believe to militate against recovery. Administration of carbon dioxide in treatment is therefore desirable for this reason, as well as for the more important reason that it stimulates the respiratory centre, thereby causing deep breathing. That the deep breathing so caused may be as completely effective as possible, oxygen should also be given. Dr. C. K. DRINKER[2] of Boston strongly advocates, and points out the advantages of, a mixture of 7 per cent. carbon dioxide and 93 per cent. oxygen. His article is one of the clearest summaries of the physiological and therapeutic aspects of carbon monoxide poisoning that we have seen, and is well worth reading.

Chronic carbon monoxide poisoning is a recurring subject of controversy, largely, as the recent advisory committee of the Royal College of Physicians of London on domestic heating by gas suggest,[3] because of confusion in terminology. DRINKER points out that acute poisoning followed by recovery may leave residual lesions. The body has been deprived of oxygen, and some parts of it, notably the nervous system, may have suffered irreparable damage. He states, and produces evidence, that this is rarer than one would expect. Acute poisoning is usually followed either by death or complete recovery, but some cases do show sequelæ. This, however, is not chronic carbon monoxide poisoning. By chronic is meant the result of continual exposure to concentrations of the gas insufficient to produce acute poisoning, and chronic poisoning in this sense is the entity which is denied existence by some, but in which others believe. The advisory committee of the Royal College of Physicians to which we have just referred hold that "the available evidence is unconvincing as to the occurrence of any definite group of symptoms which would indicate a chronic form of carbon monoxide poisoning." BECK says: "The results establish the fact that slow carbon monoxide asphyxiation (anoxæmia) produces a definite clinicopathologic entity despite views held to the contrary." At first sight these two statements appear irreconcilable, but a perusal of BECK'S paper leaves us with the impression that his patients, whose "intermittent exposure ranged from several months to eighteen years," might have been suffering from repeated attacks of slight acute poisoning. Common sense at least suggests that such a sequence of attacks might well have permanent results, and that the possibility of their occurrence (e.g., in industry) should be minimised. Such an entity, if established, would probably be known as "chronic carbon monoxide poisoning," in spite of definitions excluding it from that title.

Chronic poisoning in the sense in which we have defined it, as something gradually appearing in the complete absence of any signs of acute poisoning, probably does not exist. This point is not, as may at first appear, merely academic. Dr. J. S. OWENS,[4] for instance, in the course of a paper on carbon monoxide poisoning from motor-car fumes, mentioned in 1933 "the possibility that low concentrations of CO may be injurious when breathed for long periods," while M. LOEPER[5] and his colleagues in Paris have just published a paper on occupational CO poisoning in which they attribute various quite severe symptoms to minute but abnormal blood-CO values, only measurable by a certain chemical method more delicate than spectroscopy. In this group of patients long exposure to small concentrations of CO was established. The argument, convincing at first, is not helped by the paper immediately following, in which they describe "l'oxycarbonémie endogène." This deals with a group of patients with various clinical syndromes in which similar concentrations of CO in the blood are attributed to the effects of the malady itself and not to exposure to CO. Fortunately it is now generally admitted that carbon monoxide is chemically non-toxic, and can be injurious only in so far as it produces anoxæmia. There is no evidence that exposure which does not result in anoxæmia has the slightest effect, and even BECK'S contention that repeated anoxæmia is injurious is by no means generally accepted. Dr. ESTHER KILLICK'S recent work[6] is also reassuring, for it shows that the body, on repeated exposure to carbon monoxide, develops a resistance to it so that the blood takes up less and less on successive occasions. Though it may be an insidious enemy, carbon monoxide has no hidden resources, and can be fought very successfully if we make full use of our ordinary weapons.

Dr. A. Hugh Thompson, consulting surgeon to the Western Ophthalmic Hospital and a valued contributor to THE LANCET, died on Jan. 11th at his home in Ellerdale-road, Hampstead, in his 78th year.

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[1] *J. Industr. Hyg.* November, 1936, p. 637.
[2] See *Lancet*, 1936, **2**, 1531.
[3] *Ibid*, 1933, **1**, 154.
[4] *Bull. Soc. méd. Hôp. Paris*, Dec. 21st, 1936, pp. 1671 and 1676.
[5] See *Lancet*, 1936, **2**, 143.

THE DUBLIN FEVER HOSPITAL.—On Jan. 1st the new constitution of Cork-street Fever Hospital became effective, and the institution will in future be known as the Dublin Fever Hospital. Hitherto, the hospital, which has been in existence for more than a hundred years, has been a voluntary institution controlled by a board of voluntary governors. It was founded originally mainly by members of the Society of Friends, and there has always been a strong element of that philanthropic society interested in its management; the same family names recur again and again in the roll of governors. From the beginning of this year the voluntary character of the institution disappears and the hospital becomes a public one, the cost of maintenance being a joint charge on the corporation of Dublin and on the Dublin board of assistance. The control will be in the hands of representatives of these two bodies and of the existing board of governors of the hospital, who are constituted a perpetual college of electors for the election of such representatives. The medical officers of health for the city and the county of Dublin will have certain advisory duties in regard to the hospital. The present site is not sufficient for the enlargement required, and it is understood that search is being made for a commodious and convenient site.

ANNOTATIONS

HOSPITAL UNITY AT OXFORD

OXFORD will soon have lost the remains of her reputation as a home of lost causes. A pioneer in the hospital contributory scheme 17 years ago, she has now started a plan for the better coördinating of hospital services comparable to the one in operation at Manchester.[1] The Oxford and District Joint Hospitals Board, upon which the University, local public health authorities, and medical organisations are all represented, has been formed under Lord Nuffield as president. The primary function of the Board will be to make and keep continuous touch between the various hospitals in the area, the representatives of which will thus be able to confer often upon questions of local hospital service. One immediate and valuable effect of such liaison might be that cases which could not be admitted to one hospital, because all its beds were full, might be admitted without undue waste of time and money to another hospital not far away. The Board further suggests that appeals for contributions, at present circulated by each hospital separately, should be coördinated, thus saving expense and avoiding overlapping. Provided that subscribers may earmark their subscriptions for a particular hospital if they so wish, the Board thinks that such coördination would lead to an increase rather than a decrease of contributions. Though it must be clearly understood that the Board will in no wise attempt to tamper with the actual administration of any of the hospitals, all of which will retain their identity and independence, it is hoped that, through their representatives on the Board, the hospitals will jointly consider schemes for hospital extension or the building of new hospitals suitable for the needs of the whole area. Further matters that might in the future be considered by the Board are the supplementing of present ambulance services and the provision of further facilities for convalescent treatment. More immediately, the Board has decided to coöperate in raising funds for the Banbury Hospital rebuilding scheme. Whether or no the voluntary hospital system itself is to be looked upon as a lost cause, it still has many staunch friends; and the best way in which they can help it to survive is to make it coöperate rather than conflict with municipal services. The Oxford and District Joint Hospitals Board is a step in the right direction and it seems likely that this attempt to secure local hospital unity will not long be confined to Manchester and Oxford.

MASKS AND FACES

WHEN our daily colleague grows a beard or our wife bobs her hair it is bound to be disturbing for a while to our companionship. There is no question as to whether the new style is better or worse than the old; what upsets us is the fact of alteration, for nothing distracts us from the realities of life so much as chops and changes in its superficialities. Regular meals, a permanent Bradshaw, our own bed and old companions make for a free spirit which can go more easily and on better excursions if there is no disturbance in its temporal surroundings; the real artist of the spirit is generally a steady family man of pretty fixed habits who cannot waste his capacity for adventure on wearing strange clothes and living a curious life. So there is bound to be some emotional upset when one of the great English weeklies dresses up in new clothes, with as it happens a little lipstick thrown in. No one, except perhaps the printer, has thought of the *British Medical Journal* as a delicious example of typography, nor fondled its leaves with the affection of a bibliophile. We have known it and loved it as a faithful source of information and inspiration; we wanted to listen to its talk, and never thought whether the familiar face we liked so well was handsome or ugly. The *Practitioner* and the *Medical Press and Circular* have also had a new outfit for Coronation year, and *Nature* not long since reformed its appearance. To readers and to writers it is all rather upsetting. But they are not the only people who are in fact concerned. The artistry of legible type and the technique of printing have devotees who are equally anxious for progress, and have equivalent progress to exploit, and if the new form is easier to read by so much will it make it easier for the reader to suck up advantage. And it will not be long before the new form becomes the familiar face. It reminds us of the kindly lady who looking at the memorial plaque of her husband which was just a fiasco said, "Oh, well, of course it isn't a bit like him but people will soon believe that he was like it, so its all right." And so in the end we should be equally disturbed if the beard came off or the hair went back to a bun.

A SURGICAL ATTACK ON PSYCHOSES

THERE is at present no sign that timidity or conservatism is holding up any advance in the treatment of mental disorder. Prof. Moniz, well known for his valuable and audacious work on cerebral angiography, shows himself equally bold in attacking the problems of psychiatry. He decided, on theoretical grounds, to see what would be the effect of destroying tissues of the prefrontal region in each cerebral hemisphere of insane patients. His theoretical grounds, as presented here in detail, seem crudely neurological, naive, and faulty from the psychiatrist's point of view, but that is not an important objection if the procedure so based leads to striking benefit. Prof. Moniz modestly puts forward the opinion, shared by his distinguished Lisbon colleagues, that striking benefit has in fact followed the operation in most of the twenty cases so far treated. He gives full details of these cases—in which excitement and anxiety were the prominent clinical features—to enable the reader to form an independent opinion. It is evident that in some of his patients the mental disorder cleared up surprisingly soon after operation, and there is no reason to dispute his provisional figures—viz., seven patients recovered, seven considerably improved, and six unchanged (of whom five were schizophrenics).[1] Ten of the twenty patients were treated by injections of alcohol into the centrum ovale, ten by gouging out the tissue with a specially devised leucotome. Prof. Moniz, in his excellent account of what he did and what happened afterwards, proves his point that the operation has not had fatal or disconcerting effects, but he scarcely convinces the reader that it does more good than less heroic forms of treatment might. He is however so cautious, and even deprecating, in his gentle yet persuasive claims that others are sure to try the method and, if they follow his recommenda-

[1] *Lancet*, 1936, **2**, 1403.

[1] Tentatives opératoires dans le traitement de certaines psychoses. By Prof. Egas Moniz. Paris: Masson et Cie. 1936. Pp. 374. Fr. 40.

tion to reserve it for prolonged depressive attacks, suicidal conditions, and severe anxiety, they are also sure to obtain many recoveries which will not be decisive as to its value. In the meanwhile the monograph adds a curious chapter to the history of psychiatric treatment, and yields valuable information on what human beings can stand (e.g., in some instances the alcohol was squirted in while the patient was conscious), and on the general, neurological, and psychical effects of this trauma in the frontal lobes of the brain.

DUPUYTREN'S CONTRACTURE

Feurstein [1] suffered from Dupuytren's contracture in the ring finger of his left hand, which was bent at 20°. Having little confidence in surgical measures he decided to treat himself with radium—though he could find little to encourage him in what had been written on the subject. He divided the Y-shaped thickening of the palm into two fields, one longitudinal the other transverse, and to each field applied 50 mg. radium filtered with brass, gutta-percha, and gauze for 48 minutes (40 mg. hours). Eighteen days later he gave a half-dose, and in a further month repeated the full dose. The result delighted him. Pain disappeared, full extension of the finger became possible, and the fibrous mass diminished. Some years later he observed the same condition beginning in the right hand in the form of a tender round subcutaneous mass, the size of a pea. He applied the same treatment with equal success. After a similar experience with eight other cases he concludes that radium treatment is the method of choice for early cases though it does not give a perfect cosmetic result. Severe cases he thinks should be treated by surgery followed by radium to prevent the formation of cheloid.

STAINING OF THE RETINA IN LIFE

THE retina is translucent and the ophthalmoscope reveals only such lesions in it as are opaque to light. Examination by red-free light is the one substantial advance that has been made in revealing more than the ordinary ophthalmoscopic methods allow, but large groups of retinal affections, such as the extensive degeneration following optic atrophy, still remain invisible. The possibility of revealing these by vital staining was suggested in a paper read on Jan. 8th at the ophthalmological section of the Royal Society of Medicine by Mr. Arnold Sorsby, Dr. A. Elkeles, Dr. G. W. Goodhart, and Dr. I. B. Morris. The difficulties in such a procedure are essentially two: a dye has to be used that will pass the blood-brain barrier, and the dye has to be non-toxic. Since the experiments of Goldmann in 1913 it has been held that vital dyes do not stain the brain; in fact the clear enunciation of the blood-brain barrier theory was largely due to the failure of Goldmann and subsequent observers to get such staining. Ophthalmologists—e.g., Schnaudigel and Rados—brought forward additional evidence to this effect by their failure to stain the retina. That the barrier was not as complete as these earlier observers thought has become apparent from the work of Lina Stern and her collaborators, and it is now known that basic dyes do get through the barrier and stain the grey matter of the brain. Recent work by Fisher on the iris and ciliary body, and of Kuboki on the vessels of the choroid have added to the possibilities of vital staining in the intact animal. Working on the rabbit with basic dyes, Sorsby and his collaborators were able to obtain only transient staining in normal retinæ, but the staining was of many hours' duration if the retina was first damaged by chemical or mechanical means. They demonstrated to the society a series of rabbits in which they had produced pigmentary degeneration of the retina by the intravenous injection of Septojod, an iodine preparation, and also a rabbit with thermal injury to one retina. Such rabbits showed staining of the fundus when subjected to intravenous or intramuscular injection of light green and other dyes, the depth of staining bearing a direct relationship to the degree of injury. The mechanism appears to be that the normal retina can oxidise the dye to a colourless leuco-base, while the damaged retina has lost most of this ability. Should it prove possible to apply these results clinically there seems a prospect that the pathological retina may be rendered visible. No less important would be the emergence of what promises to be a method for the study of retinal metabolism.

THE MOVEMENT FOR BIRTH CONTROL

THE annual report of the National Birth Control Association for the year 1936–37 has reached us, and provides evidence that its work has been progressive in many directions. The two primary objects of the Association are: (1) the provision by local authorities of advice for women whose health makes pregnancy medically undesirable; and (2) the provision of voluntary clinics for women whose circumstances are such that both public policy and their individual good demand family limitation. In both cases those whoo ppose the spread of contraception point to a falling birth-rate, and to them the introduction to the report supplies a considered reply. The words of Lord Dawson in the House of Lords are quoted, when he said: "It is a fact that the smaller families of to-day have a higher proportion of fitter children and the mothers of those children are as well as, and in my judgment better than, those of any previous generation." Similar support of the movement has been advanced by Lord Horder who has publicly stated that a sane population policy must include planned families.

It seems to be generally recognised that the population of Great Britain will shortly become stationary before declining, and the report of the Association holds that this is exactly the place where birth control clinics would play an important part by making parenthood easier, and by reducing the mortality-rates of infants and mothers. That these arguments are prevailing is shown by the increasing number of medical men who support the Association and by the statement that during the year under consideration 18 new clinics have been established, while 23 more maternity and child welfare authorities have decided to refer cases either to clinics, whose number is increasing, or to doctors in private practice. Good practical work has been done by the Birth Control Investigation Committee of the Association, the activities of which have been supported by grants from the Eugenics Society. Under this committee, Dr. J. R. Baker, working in the department of pathology, Oxford University, has continued his researches into the spermicidal substances which were reported in his recent book "The Chemical Control of Conception." [1] Dr. S. Zuckerman, working in the department of human

[1] Feurstein, J. G. (1936) *Wien. klin. Wschr.* **49**, 1090.

[1] *Lancet*, 1936, **1**, 1071.

anatomy, Oxford University, has been engaged upon a general inquiry into the factors concerned with the period of fertility in primates. Among other things, he has been concerned in investigating the time of ovulation in primates, the variability of the phases of the menstrual cycle, the cyclical excretion of the sex hormones, and the physiology of sexual-skin swelling. He has further been able to conduct a limited number of controlled matings with a view to ascertaining the limitations of the period of fertility occurring within the cycle.

A satisfactory financial position was reached during the year owing, apparently, to the success of a gala-ballet performance, the receipts from which transformed a probable deficit into a credit balance. But with the development of the work for the coming year, larger support will be required, while there is proof that when a clinic is opened special donations are received; this means that if money is spent money is forthcoming. All who read the report will learn how and why further financial support is necessary, and the work recorded in the report of the Association justifies the plea for substantial assistance.

FATALITIES ATTRIBUTED TO NITROUS OXIDE

"LAUGHING-GAS" has so long been regarded as an anæsthetic—perhaps the only one—which has no poisonous properties that attention is at once attracted by the record of fatalities attributed to its direct action. It is true that plenty of deaths have followed the use of the gas; but this is bound to happen when an anæsthetic is often chosen, because it is innocuous, for patients who are gravely ill or are to undergo some especially trying operation. Deaths in these circumstances have been explicable without assuming any toxic effect from the anæsthetic itself. Some cardiac dilatation has indeed been put down to nitrous oxide, and the late Dudley Buxton believed it sometimes responsible for this complication. The fatalities, however, now recorded [1] are in quite a different category, for in two of the three cases the operations were trivial. There appears to be here no question either of asphyxia—which is of course easily caused by improper giving of nitrous oxide—or of death from surgical shock. In none of the cases did post-mortem examination reveal to the naked eye any cause of death, and it was on the histological existence of damage to the cortex of the brain that the verdict is based of "death from destruction of cerebral cortex following nitrous oxide and oxygen anæsthesia." Details of the damage are given: it was mainly in the deeper layers of the cortical cells; the neurones of all layers below the top were somewhat affected, those of the lowest layers being wholly destroyed. The parenchyma of the basal ganglia also showed severe degenerative changes, but the cells were only slightly reduced in number. A fourth patient of whom a record is given recovered, although not completely, after eight months of various pareses.

These records are unusual and alarming. Moreover, there is this difficulty in understanding the sequence of events as represented—that if the deaths and the early symptoms were due to the cerebral damage this must have started with rapidity early in the inhalation. That creates a new conception of the possible effects of nitrous oxide, and will not probably be accepted forthwith solely on the histological evidence from patients all of whom died many hours after the inhalation had ceased. The symptoms in two of the cases started about twenty minutes after the beginning of the inhalation, with spasm and jerking of limbs and stoppage of breathing. This was started again artificially but neither recovered consciousness, and they died 60 and 74 hours from the start, after incontinence and abolished reflexes had been noted. The fourth patient, who recovered, was the only one of the series whose operation was a long one. He was under the anæsthetic for an hour and a half, and the symptoms began an hour later.

[1] Lowenberg, K., Waggoner, R., and Zbinden, T.: *Ann. Surg.* November, 1936, p. 801.

CHILDREN IN WINTER

WRITING on the care of children in winter, Dr. Alan Moncrieff [1] recommends that they should go out daily, in any weather except fog, between 11 A.M. and 1 P.M. to make the most of the sun. Children of four and under should go to bed at 6 P.M., half an hour's grace for each year of age being allowed to older children, with 8 P.M. as the limit for all children under thirteen. The rest period, unless it can be taken in the open air, should not clash with the outing period. Fresh air is essential by day and night and rooms must not be overheated, dry, or dusty. By night, small restless children should wear a jersey or pullover; for the daytime Moncrieff suggests a woollen vest next the skin and woollen socks, a woollen jersey, or frock with woollen knickers for girls, and trousers for boys. Bare knees are desirable indoors, but woollen pullovers to cover the whole of the legs should be worn out of doors by young children. He does not object to gloves for those who feel the cold in their hands, and the most important point about footgear, he thinks, is that the soles should be waterproof. Wet clothes, especially wet shoes, should be changed at once and dry slippers should be kept for use at school. There is much to be said for wind-resisting garments; but hats, unless the child has grown accustomed to wearing them, are unnecessary. A little extra food to compensate for heat-loss is needed in winter. Extra fat, in the form of butter—preferably butter produced in those parts of the world where the sun shines in winter—is excellent and its effect in producing acidosis has, he thinks, been exaggerated. A bowl of porridge, or other cereal, enriched by cream, butter, or vitaminised margarine, makes a sound breakfast for children in winter. Green vegetables, salads, fruit, liver, fish, and fish-roes are all good, and extra milk, provided that it is "safe," should only be withheld from children with poor appetites. With a diet generously planned on these lines added vitamins are unnecessary. Ten per cent. of colds are "home-grown" and are amenable to treatment of ear, nose, and throat, surgical or otherwise. The remaining 90 per cent. are caught from another sufferer. In Moncrieff's opinion vaccines and ultra-violet radiation are useless against colds and attempts must be made to increase the child's resistance by sound feeding and avoidance of fatigue or chilling. Cold baths or cold sponging all the year round may have a hardening effect. Diphtheria, measles, scarlet fever, and whooping-cough are all more prevalent in winter. All children should be protected against diphtheria by injection in the second or third year of life. Mild attacks of measles can be assured by the use of convalescent serum and scarlet fever responds well to serum treatment. Whooping-cough is now probably the greatest problem, though vaccine prophylaxis may yet prove a success. Rickets persists as a

[1] *J. State Med.* January, 1937, p. 50.

characteristically winter ailment because cod-liver oil is given in too small doses. Emulsions are dilute, containing at best only 50 per cent. of cod-liver oil, while "cod-liver oil and malt" may contain only 10 per cent. A child a month old requires a few drops daily of pure cod-liver oil; at six months, a teaspoonful daily is necessary; and at a year one and a half or two teaspoonfuls. The maximum dose is required in winter and only slightly less should be given in summer if rickets is to be prevented or cured.

MYOPIA IN CHILDHOOD

THE comparative importance of heredity and environment in the genesis of myopia still gives rise to argument. The evidence published in 1867 by Hermann Cohn of Breslau made it seem that faulty environment is the usual cause of myopia in school-children and his influence did much to improve the conditions they worked under. Of late years the movement back to heredity has gained many adherents, including Steiger, who based his conclusions on a study of 50,000 eyes. The latest contribution to the discussion comes from Stockholm, where Dr. Gunnar Nordgren[1] rivals his two predecessors in the wealth of his material. Since 1894 the Swedish school authorities have kept records of the incidence of myopia, and though only 14,000 children were examined in 1895, their numbers have risen considerably, being 27,000 in 1918. The first and perhaps the most striking observation that Nordgren discusses is the decline of myopia by about a third between 1894 and 1920. It may well have been a more than accidental coincidence, he thinks, that far-reaching reforms in school hygiene were introduced during this period. Between 1920 and 1935, however, there was little reduction. In analysing the possible causes no significant relationships could be established between the frequency of myopia on the one hand and geographical factors, including life in town and country, on the other. Nor did myopia appear to be associated with poor physique. On the positive side was a possibly significant relationship between myopia and the general sickness-rate, but Nordgren hesitates—and indeed never completely recovers from his hesitation—over the inwardness of this association, His cautious verdict is that "there can hardly be any doubt that both predisposition and external circumstances play a part in the origin of myopia, but we have still to ask how great is the average frequency of myopia which can be traced to external factors." But later he adds: "one can, however, probably by an unimpeachable general hygiene, both in school and home, limit the extent of myopia to this irreducible minimum." This agrees with our own modest conclusion a year ago[2] that "with our present knowledge (or ignorance) it would be unwise to tamper with the principle on which most young myopes are now treated or to discourage efforts to secure special care for myopic children."

MERCURIAL ANTISEPTICS

WITH the title of "The mechanism of inactivation of mercurial antiseptics by serum and its implications regarding the possibility of intravenous antisepsis," Smith, Czarnetzky, and Mudd[3] have published an excellent study of which our only criticism is that it seems somewhat belated. Their method was to determine the proportion of surviving bacteria at a series of time intervals in mixtures of diluted culture with solutions of mercuric chloride, mercurochrome, merthiolate, and a compound said to be identical with Metaphen, with and without the addition of 80 per cent. of normal horse serum. In the presence of serum the concentration of mercuric chloride had to be multiplied by 300 to obtain the bactericidal effect exerted in its absence, that of metaphen 400 times, of mercurochrome—which was in any case by far the weakest germicide of the four—800 times, and of merthiolate 14,000 times. These differences are of course due to the combination of mercury with serum protein, and it is deduced from comparison of different curves of survival-rates that this combination takes place faster than the reaction with bacteria which is responsible for germicidal effect. Further purely chemical experiments were undertaken to determine how much of these compounds will combine with a given quantity of serum protein, and for each of them it was found that this amount was approximately 0·35 gramme as mercury per litre of serum; it was further shown that this mercury-protein combination has itself scarcely a trace of bactericidal activity. No experiments are recorded in which whole blood was used in place of serum; it has been the experience of others that in this medium mercury compounds are incapacitated even further. The conclusion that these substances are "unsuitable" for intravenous antisepsis is therefore a very moderate one, and it has been reached before by other means, though perhaps not by so devastating and complete an exposure of the underlying fallacy. This might appear to be beating a dead horse, but for the fact that misguided enthusiasm and ill-chosen technique have led to fantastic claims being made on behalf of some of these mercury compounds within quite recent times. The authors are careful to say that their conclusions have no bearing on types of use other than intravenous injection; the possible merits of mercury compounds for superficial disinfection are quite another problem.

POSITIVE AND NEGATIVE

THE ordinary man—and some say that doctors are the most ordinary of men—usually finds it hard to appreciate that the active disease he is observing is not caused by some equally active and positive noxious influence. The discoveries of the early bacteriologists undoubtedly supported this attitude of mind, in that they were so often able to produce (on demand) microbes, toxins, and what-not out of their conjurors' flasks. The conception of some negative factor as a cause of disease took a long time to be established and even now it is not always easy to revise our ideas of pathology to keep pace with the discoveries in the field of vitamin research. It is annoying to be told for instance that alcoholic polyneuritis has nothing to do with alcohol, but is the result of a vitamin-B deficiency. Yet this appears to be so. At all events, Dr. M. B. Strauss in the Harvard tercentenary symposium on nutrition[1] stated that patients could be cured of their neuritis by changing their diets but without restricting their whisky. It was suggested also that the so-called toxic polyneuritis of pregnancy can be cured by administering vitamin B, as G. W. Theobald has maintained in our own columns[2]; which would make it improbable that even this polyneuritis is really

[1] *Nord. med. Tidskr.* Dec. 19th, 1936, p. 2069.
[2] *Lancet*, 1935, **2**, 1418.
[3] Smith, D. E., Czarnetzky, E. J., and Mudd, S., *Amer. J. med. Sci.* December, 1936, p. 790.

[1] *New Eng. J. Med.* Dec. 17th, 1936.
[2] *Lancet*, 1936, **1**, 834.

toxic in origin. Strauss's contribution was but one of a series, almost all of which emphasise some relationship between disease and defective nutrition. The symposium as a whole is a mixed bag, but it illustrates very well the trend of current thought. "Deficiency" has quite displaced "toxins" in the minds of the investigators; and this is an excellent thing, for hypothetical toxins were a sterilising conception and have never provided us with a satisfactory basis for treatment, whereas proved deficiencies offer great therapeutic possibilities.

HOSPITALS AND THE UNIVERSITY GRANTS COMMITTEE

THE work of the University Grants Committee provided the subject for a meeting of the University and Research Section of the Library Association on Saturday last. Mr. R. Offor, Ph.D., librarian of Leeds University, who opened the discussion, and other speakers were unanimous in their testimony to the freedom from red tape in the Committee's work. They all agreed about the value of the quinquennial visits of the Committee to discuss on the spot with representatives of the universities their problems and needs. It is for these reasons that friends of voluntary hospitals have looked to an extension of the powers of the Committee in the direction of giving financial assistance to the actual work of the hospitals. Something of the kind seems to have been in the mind of the Scottish public health services committee in proposing a "teaching faculties grant." With the extension of opportunities for medical education in the council hospitals such a grant could however hardly be confined to voluntary hospitals, and in England it could not extend to the many voluntary hospitals which have no connexion with a medical school. It must too be remembered that the University Grants Committee is concerned with the medical school rather as a part of the university than as an adjunct to a hospital. Hence we think it very doubtful that the University Grants Committee will consider it within the scope of its duties to come to the financial support of voluntary hospitals. None the less, those hospitals will join with the Library Association in their tribute to the Committee.

HENRY TONKS

Prof. Henry Tonks, who died at his house in Chelsea on Friday last, Jan. 8th, was rightly famous as artist and teacher, and his first impulses in those directions were received while he was a medical man, and attached to the medical school at the London Hospital. He gained the diploma of F.R.C.S. Eng. in 1888, and was for a time assistant demonstrator of anatomy in the medical school of "the London," while he held house appointments at the hospital and at the Royal Free Hospital, where he was for a time senior resident medical officer. His first direct step from one profession to another was taken when he became lecturer on artistic anatomy at the Westminster School of Art, and Prof. Brown, when he moved from the Westminster to the Slade School, invited Tonks to become his assistant. From this time forward Tonks gave up the pursuit of medicine and devoted himself entirely to painting and its teaching. In 1917 he was elected Slade professor of fine art in the University of London in succession to Prof. Brown, a position which he held for thirteen years to the great advantage of those with the pursuit of their studies at heart, and to the discomfiture of any who thought either that drawing was easy or that accomplishment could be achieved in accordance with some set of precepts. He was from the beginning associated with the New English Art Club, where his contributions were welcomed by a rather select group of admirers. Otherwise he rarely exhibited his work, but several examples can be seen in the Tate Gallery, and in this gallery a special exhibition of his work was held last October. This was a high tribute to his output and his ideals.

During the war Tonks returned to medicine, doing certain surgical work abroad, and especially acting as an artist. Here both his artistic and surgical qualities were displayed in a series of pictures of the victims of facial injuries who were treated at Sidcup. These pastels were usually drawn in two stages, the first showing the injuries to be treated and the second the results of treatment, but occasionally Tonks's detailed knowledge of anatomy would emerge in an outline drawing for the scheme of restitution. Seventy-two of these pictures—69 pastels and 3 pen-and-ink drawings—are included in the army medical section preserved in the museum of the Royal College of Surgeons of England. They form a striking testimonial to Tonks's masterful drawing, while the humanity of their object mitigates their terror.

SUSCEPTIBILITY OF CHILDREN TO LEPROSY

Marchoux and Chorine[1] contend that children are not more susceptible to leprosy than adults, but owing to their inexperience and other circumstances of childhood are more likely to be exposed to infection. This opinion they base on the analogy of rat leprosy. They found that adult rats are as easily infected as new-born rats by contact with leprous animals which show bacillus-bearing ulcers; the infection apparently goes through the conjunctiva and attacks first Harder's gland at the inner canthus and afterwards the adjacent sublingual and submaxillary lymph glands. When rat leprosy was induced by inoculating bacilli into the skin it was noted that the speed and severity of the infection increased with the dose of organisms and the size of the area over which they were distributed. It is concluded therefore that the apparently increased susceptibility of children to Hansen's organism is due to their greater exposure, and the greater likelihood of infection entering over a large skin surface because of their close contact, naked, with their infectious parents.

The question arises, however, how far it is justifiable to argue from rat leprosy to human leprosy. True the two diseases resemble each other in some respects: Hansen's bacillus and Stefansky's bacillus are similar in morphology and staining reactions; both are difficult or impossible to cultivate in vitro; and progressive disease has been produced by each in only one genus. But the most characteristic feature of human leprosy is the affinity of *B. lepræ* for the peripheral nerves, and this is apparently absent in rat leprosy. The contention that children are not more susceptible to leprosy than adults is not borne out by the leprolin test, which (there is good reason to believe) gives a delicate indication of the protective response of the human skin to invasion by Hansen's bacilli. Compared with that of adults the skin of children reacts much less to intradermal injection of a sterilised suspension of leproma, and this variation of reaction probably has an important bearing on resistance in early and later life.

[1] Marchoux, E., and Chorine, V., *Ann. Inst. Pasteur*, December, 1936, p. 583.

PRINCIPLES OF MEDICAL STATISTICS

III.—PRESENTATION OF STATISTICS

In dealing with a series of observations the first object must be to express them in some simple form which will permit, directly or by means of further calculations, conclusions to be drawn. The publication, for instance, of a long series of case results is not particularly helpful (beyond providing material for interested persons to work upon), for it is impossible to detect from the unsorted mass of raw material relationships between the various factors at issue. The worker must first consider the questions which he believes the material is capable of answering, and then determine the form of presentation which brings out the true answers most clearly. For instance, let us suppose the worker has amassed a series of after-histories of patients treated for gastric ulcer and wishes to assess the value of the treatment given, using as a measure the amount of incapacitating illness suffered in subsequent years. There will be various factors, the influence of which it will be of interest to observe. Is the age or sex of the patient material to the upshot? Division of the data must be made into these categories and tables constructed to show how much subsequent illness was in fact suffered by each of these groups. Is the after-history affected by the type of treatment? A further tabulation is necessary to explore this point. And so on. The initial step must be to divide the observations into a relatively small series of groups, those in each group being considered alike in that characteristic for the purpose in hand. To take another example, in the Table showing the fatality-rate from scarlet fever of hospital cases, children within each year of age up to 10 and in each five-year group from 10 to 20 are considered alike with respect to ages.

Table showing Hospital Cases of Scarlet Fever, 1905–14

Fatality-rate at ages

Age in years.	Number of cases.	Number of deaths.	Fatality-rate (%).
0–	46	18	39·1
1–	383	43	11·2
2–	881	50	5·7
3–	1169	60	5·1
4–	1372	36	2·6
5–	1403	24	1·7
6–	1271	22	1·7
7–	986	21	2·1
8–	864	6	0·7
9–	673	5	0·7
10–	1965	14	0·7
15–20	513	3	0·6

The fatality, or case-mortality, rate is the proportion of patients with a particular disease who die.

It is, of course, possible that by this grouping we are concealing differences. The fatality-rate at 0–6 months may differ from the fatality-rate at 6–12 months, at 12–18 months it may differ from the rate at 18–24 months. To answer that question further subdivision—if the number of cases justifies it—would be necessary. In its present form (accepting the figures of hospital cases at their face value) the grouping states that fatality declines nearly steadily with age, a conclusion which it would be impossible to draw from the 11,526 original unsorted and ungrouped records. The construction of a *frequency distribution* is the first desideratum—i.e., a table showing the frequency with which there are present individuals with some defined characteristic or characteristics.[1]

As a general rule the distribution should be drawn up on a fine basis—i.e., with a considerable number of groups, for if this basis prove too fine owing to the numbers of observations being few, it is possible to double or treble the group-interval by combining the groups. If, on the other hand, the original grouping is made too broad, the subdivision of the groups is impossible without re-tabulating much of the material.

Statistical Tables

To return to the original table, this may be used in illustration of certain basic principles in the presentation of statistical data.

(i) The contents of the table as a whole and the items in each separate column should be clearly and fully defined. For lack of sufficient headings, or even any headings at all, many published tables are quite unintelligible to the reader without a search for clues in the text (and not always then). For instance, if the heading given on the left of the table were merely "age," it would not be clear whether the groups refer to years or months of life. The unit of measurement must be included.

(ii) If the table includes rates, the base on which they are measured must be clearly stated—e.g., death-rate per cent., or per thousand, or per million, as the case may be (a very common omission in published tables). To know that the fatality-rate is "20" is not helpful unless we know whether it is 20 in 100 patients who die (1 in 5) or 20 in 1000 (1 in 50).

(iii) Whenever possible the frequency distributions should be given in full. These are the basic data from which conclusions are being drawn and their presentation allows the reader to check the validity of the author's arguments. The publication merely of certain values descriptive of the frequency distribution—e.g., the arithmetic mean or average, severely handicaps other workers. For instance, the information that the mean age at death of patients with cancer of the lung is 54·8 years and with cancer of the stomach is 62·1 years is of very limited value in the absence of any knowledge of the distribution of ages at death in the two classes.

(iv) Rates or proportions should not be given alone without any information as to the numbers of observations upon which they are based. In presenting experimental data, and indeed nearly all statistical data, this is a fundamental rule (which, however, is constantly broken). For example, the fatality-rate from small-pox in England and Wales (ratio of registered deaths to notified cases) was 42·9 per cent. in 1917, while in the following year, 1918, it was only 3·2 per cent. This impressive difference becomes less convincing of a real change in virulence when we note that in 1917 there were but 7 cases notified, of whom 3 died, and in 1918 only 63 of whom 2 died.

[1] The choice of groups and the group-intervals and the calculation of averages and other values from such distributions are discussed in numerous text-books of statistical method—e.g., Woods and Russell: An Introduction to Medical Statistics. London: P. S. King and Son. 1936.

(Though the low rate of 1918 *may* mark the presence of variola minor.) "It is the essence of science to disclose both the data upon which a conclusion is based and the methods by which the conclusion is attained." By giving only rates or proportions (and by omitting the actual numbers of observations or frequency distributions) we are excluding the basic data. In their absence we can draw no valid conclusion whatever from, say, a comparison of two, or more, percentages. Even when the number of observations is small, 20–25 perhaps, there is no reason why a percentage distribution or a rate should not be calculated but, as discussed later, particular care will have to be exercised in drawing conclusions.

(v) Full particulars of any deliberate exclusions of observations from a collected series must be given, the reasons for and the criteria of exclusion being clearly defined. For example, if it be desired to measure the success of an operation for, say, cancer of the breast, it might, from one aspect, be considered advisable to take as a measure the percentage of patients surviving at the end of 5 years *excluding those who died under the operation itself*—i.e., the question asked is "what is the survival-rate of patients upon whom the operation is successfully carried out?" It is obvious that these figures are not comparable with those of observers who have included the operative mortality. If the exclusion that has been made in the first case is not clearly stated, no one can necessarily deduce that there is a lack of comparability between the records of different observers, and misleading comparisons are likely to be made. Similarly one worker may include among the subsequent deaths only those due to cancer and exclude unrelated deaths—e.g., from accident—while another includes all deaths, irrespective of their cause. Definition of the exclusions will prevent unjust comparisons.

Sometimes exclusions are inevitable—e.g., if in computing a survival-rate some individuals have been lost sight of so that nothing is known of their fate. The number of such individuals must invariably be stated and it must be considered whether the lack of knowledge extends to so many patients as to stultify conclusions. For instance, if 1000 patients were originally observed, 300 are known to be dead at the end of 5 years, 690 are known to be alive, and 10 have been lost sight of, this lack of knowledge cannot appreciably affect the survival-rate. At the best, presuming the 10 are all alive, 70 per cent. survive (700 out of 1000); at the worst, presuming the 10 are all dead, 69 per cent. survive (690 out of 1000). But if 300 are known to be dead, 550 are known to be alive, and 150 have been lost sight of, the upper and lower limits are 70 per cent. surviving (700 out of 1000, presuming the 150 are all alive) and 55 per cent. surviving (550 out of 1000 presuming the 150 are all dead), an appreciable difference. To measure the survival-rate on only those patients whose history is known, or, what comes to the same thing, to divide the 150 into alive and dead according to the proportions of alive and dead in the 850 followed up successfully, is certainly dangerous. The characteristic "lost sight of" *may* be correlated with the characteristics "alive or dead"; in other words, a patient who cannot be traced may be more likely to be dead than a patient who can be traced (or vice versa), in which case the ratio of alive to dead in the untraced cases cannot be the same as the ratio in the traced cases. Calculation of the possible upper rate shows at least the margin of error.

Beyond these few rules it is very difficult, if not impossible, to lay down laws for the construction of tables. The whole issue is the arrangement of data in a concise and easily read form. In acquiring skill in the construction of tables probably the best way is, as Pearl suggests, to consider critically published tables with such questions as these in mind: "What is the *purpose* of this table? What is it *supposed* to accomplish in the mind of the reader? . . . wherein does its failure of attainment fall?"[2] Study of the tables published by the professional statistician—e.g., in the Registrar-General's Annual Reports—will materially assist the beginner.

Graphs

Even with the most lucid construction of tables such a method of presentation always gives difficulties to the reader, especially to the non-statistically-minded reader. The presentation of the same material diagrammatically often proves a very considerable aid and has much to commend it if certain basic principles are not forgotten.

(i) The sole object of a diagram is to assist the intelligence to grasp the meaning of a series of figures by means of the eye. If—as is unfortunately often the case—the eye itself is merely confused by a criss-cross of half a dozen, or even a dozen, lines, the sole object is defeated. The criterion must be that the eye can with reasonable ease follow the movement of the various lines on the diagram from point to point and thus observe what is the change in the value of the ordinate (the vertical scale) for a

[2] Raymond Pearl: Medical Biometry and Statistics. Philadelphia and London: W. B. Saunders Co., Ltd., 2nd ed., 1930.

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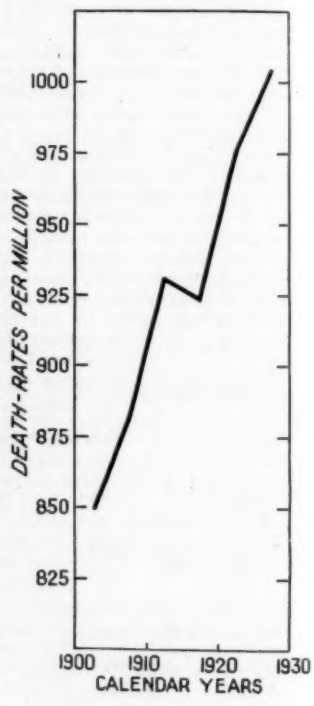

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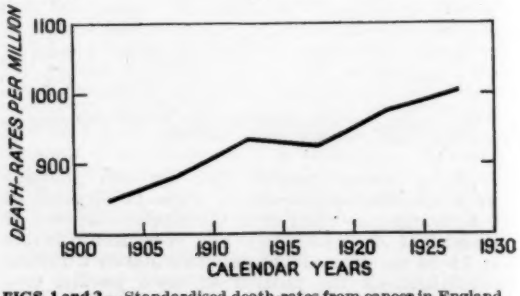
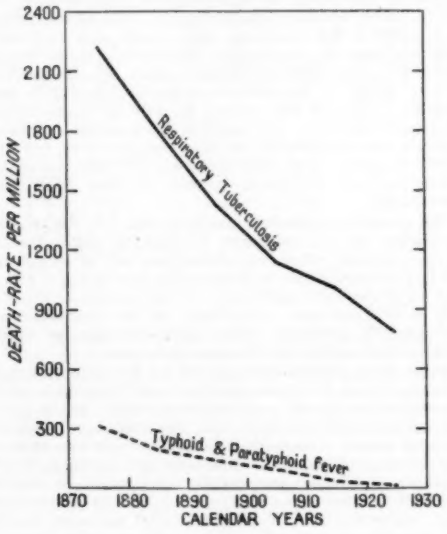


FIGS. 1 and 2.—Standardised death-rates from cancer in England and Wales in each quinquennium from 1901–05 to 1926–30.

given change in the value of the abscissa (the horizontal scale).

(ii) The second point to bear in mind in constructing *and in reading* graphs is that by the choice of scales the same figures can be made to appear very different to the eye. Figs. 1 and 2 are an example. Both show the same figures—namely, the death-rates (standardised) from cancer in England and Wales in each quinquennium between 1901 and 1930. In Fig. 1 the increase in mortality that has been recorded appears at a cursory glance to be exceedingly rapid and of serious magnitude, while in Fig. 2 a slow and far less impressive rise is suggested. The difference is, of course, due to the difference in the vertical and horizontal scales. In reading graphs, therefore, the scales must be carefully observed and the magnitude of the changes interpreted by a rough translation of the points into actual figures. In drawing graphs undue exaggeration or compression of the scales must be avoided, and it must be considered whether a false impression is conveyed, as quite frequently happens, if the vertical scale does not start at zero but at some point appreciably above it. Graphs should always be regarded as subsidiary aids to the intelligence and *not* as the evidence of associations or trends. That evidence must be largely drawn from the statistical tables themselves. It follows that graphs should never be a *substitute* for statistical tables. An entirely deaf ear should be turned to such editorial pleading as this: "if we print the graphs would it not be possible to take some of the tables for granted? Having given a sample of the process by which you arrive at the graph is it necessary in each case to reproduce the steps?" The retort to this request is that statistical tables are *not* a step to a diagram, they are the basic data. Without these basic data the reader cannot adequately consider the validity of the author's deductions, and he cannot do any further analysis of the data, if he should wish, without laboriously and inaccurately endeavouring to translate the diagram back into the statistics from which it was originally constructed (and few tasks are more irritating).

3



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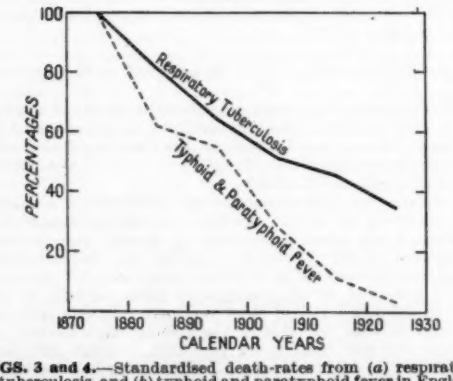

FIGS. 3 and 4.—Standardised death-rates from (*a*) respiratory tuberculosis, and (*b*) typhoid and paratyphoid fever in England and Wales. In Fig. 4 the rate from each disease in each decade is expressed as a percentage of the corresponding rate in 1871–80.

The problem of scale illustrated in Figs. 1 and 2 is also an important factor in the comparison of trend lines. Fig. 3 shows the trend of the death-rates from respiratory tuberculosis and from typhoid fever in England and Wales from 1870 to 1930. Unless the scale of the ordinate (the vertical scale) is carefully considered, the inference drawn from this graph might well be that *relatively* the mortality from respiratory tuberculosis has declined more than the mortality from typhoid fever. Actually the precise reverse is the case—relatively typhoid fever has declined considerably more than respiratory tuberculosis. In 1921–30 the rate from respiratory tuberculosis was 34 per cent. of the rate recorded in 1871–80, while the rate from typhoid fever was but 3·4 per cent. of its earlier level. *Absolutely* respiratory tuberculosis shows the greater improvement (from 2231 deaths per million in 1871–80 to 768 in 1921–30, compared with 321 and 11 for typhoid fever); but relatively typhoid fever shows the advantage. If it is the relative degree of improvement that is at issue Fig. 3 is insufficient. For this purpose the rates in each decade may be converted into percentages based upon the rate in the first decade, as is shown in Fig. 4.

It is a sine qua non with graphs, as with tables, that they form self-contained units, the contents of which can be grasped without reference to the text. For this purpose inclusive and clearly stated headings must be given, the meaning of the various lines indicated, and a statement made against the ordinate and abscissa of the characteristics to which these scales refer (vide Figs. 1 to 4).

Summary

For the comprehension of a series of figures tabulation is essential; a diagrammatic representation (*in addition to tables but not in place of them*) is often of considerable aid. Both tables and graphs must be entirely self-explanatory without reference to the text. As far as possible the original observations should always be reproduced (in tabulated form showing the actual numbers belonging to each group) and not given only in the form of percentages—i.e., the percentages of the total falling in each group. The exclusion of observations from the tabulated series on any grounds whatever must be stated, the criterion upon which exclusion was determined clearly set out, and usually the number of such exclusions stated. Conclusions should be drawn from graphs only with extreme caution and only after careful consideration of the scales adopted.

A. B. H.

SPECIAL ARTICLES

THE RELATIVE AS DONOR

CHANCES OF COMPATIBILITY

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Now that blood transfusion is a common event, and continuous transfusions are being increasingly used, it is often necessary to summon such relatives as are healthy, willing, and available for tests of compatibility as donors. In many cases the number of such relatives may be small and the husband (or wife) or a friend may offer instead. It seemed of interest to calculate the probability that a relative would be compatible, and what relationship would be the most favourable. Would a brother be less likely to be compatible than a son or a father, and how would they compare with the husband or other unrelated person in chances of compatibility? The results obtained are given below (Tables I. and II.), and details of the method of calculation follow. It should be realised that the results are theoretical and not experimental.

TABLE I

Percentage Chance of Suitability when the Donor is to be of the Patient's Own Blood Group

Patient's group.	Donor—			
	Father or mother.	Brother or sister.	Son or daughter.	Unrelated.
	Per cent.	Per cent.	Per cent.	Per cent.
I. (AB) ..	18	34	16	3
II. (A) ..	66	69	66	43
III. (B) ..	39	47	41	7
IV. (O) ..	68	71	68	46
Average, whole population ..	64	67	64	41

II

Percentage Chance of Suitability when the Donor is to be of any Compatible Group

I. (AB) ..	100	100	100	100
II. (A) ..	95	95	95	90
III. (B) ..	72	74	73	54
IV. (O) ..	68	71	68	46
Average, whole population ..	81	82	81	67

METHOD OF CALCULATION

The probability will depend upon the mechanism of inheritance of the blood groups, and upon the actual frequency of the various groups in the population in question.

The present calculation ignores cases in which serum of one group is found to agglutinate cells, apparently of the same or compatible group, on direct matching.

Bernstein's theory of the inheritance of the blood groups (Bernstein 1924, 1925) is taken as the basis of the calculation. This theory states, in effect, that the blood group of an individual is determined by his possession of a pair of genes, one derived from each parent, while each of the genes is one of three possible types, A, B, or R. The six possible pairs are thus A + B (written AB), AA, AR, BB, BR, and RR, the order of the genes in the pair being irrelevant. Blood Group I. consists of all who possess both an A and a B gene—i.e., type AB. Blood Group II. consists of all who possess an A but no B gene, and thus includes both types AA and AR. Blood Group III. consists of all who possess a B but no A—i.e., types BB and BR. Blood Group IV., consisting of those who possess neither A nor B genes, consists of type RR.

Each parent passes on to his child one or other of his two genes. Thus the children of the mating AA × BB are all AB (Group I.), while the children of the mating AR × BR are AB, AR, BR, and RR in equal proportions.

The frequency of the various blood groups in the English population has been established (Hirzsfeld 1919). It is also possible (Wiener 1934) from these frequencies, and assuming the population to be well mixed by marriage, to separate the Group II. frequency into the respective frequencies of its two parts corresponding to AA and AR, and similarly for Group III.

The actual figures obtained are as follows :—

TABLE III

Group	I. ..	AB— 3·1 per cent. of population.	
"	II. ..	AA— 7·2	" "
		AR—36·2	" "
"	III. ..	BB— 0·27	" "
		BR— 6·9	" "
"	IV. ..	RR—46·4	" "

Now, once it is known that a patient is, say, Group IV., it is easy to calculate the likelihood that a child is Group IV., and so compatible, assuming that a man's choice of wife is independent of her blood group. Thus supposing the patient to be a Group IV. man, 46·4 per cent. of all possible wives are also Group IV., and all the children of this RR × RR marriage will be RR and compatible with the patient. A further 36·2 per cent. of possible wives are type AR, of which match the children are equally likely to be AR (incompatible) and RR (compatible). Thus of this match, in half the possible cases (18·1 per cent.) the child will be compatible. Similarly the wife may rarely (6·9 per cent. chance) be of type BR, of which match half the children will be compatible, adding a 3·45 per cent. chance of the child being compatible.

The other three possible matings, with AB, AA, and BB, contribute no RR children compatible with the RR father. Adding these probabilities of a compatible child, it is found that, corresponding to the full "100 per cent. of wives," 46·4 per cent. + 18·1 per cent. + 3·4 per cent. = 67·9 per cent. of children will be compatible with a Group IV. patient. This argument applies equally whether the patient is a male or a female.

When the patient is of Group II. (or III.) the calculation is longer, since it is necessary to take into account the fact that of Group II. patients 17 per cent. are type AA and 83 per cent. are type AR, the children differing in the two cases. Proceeding as before, and remembering that AA and AR bloods are identical in their agglutination reactions, and hence compatible, the figures are obtained that an AA patient has a 94·8 per cent. chance of a Group II. child, while an AR patient has a 60·8 per cent. chance. The average chance of a Group II. patient having a Group II. child is thus the average between 94·8 per cent. and 60·8 per cent. in the ratio of the frequencies of AA and AR, giving :—

$$\frac{17}{100} \times 94{\cdot}8 \text{ per cent.} + \frac{83}{100} \times 60{\cdot}8 \text{ per cent.} = 66{\cdot}4 \text{ per cent.}$$

This method of calculation is available both for children of the same group, and for children of any compatible group. For a Group II. patient, the first calculation adds up the chances of a Group II. child; the second, the chances of a Group II. or IV. child.

For estimating the chance of compatibility of a parent, the analysis is rather similar. Assuming again that mating takes place regardless of group, the average frequency of any particular mating can be estimated. Thus the frequency of an AB individual being 3·1 per cent., in 3·1 per cent. of all matings the husband will be AB, and in 3·1 per cent. *of these* matings the wife will also be AB, so that the AB × AB mating occurs with frequency 3·1 per cent. × 3·1 per cent. = 0·096 per cent. Similarly the AB husband–AR wife mating has frequency 1·1 per cent. as has also the AB wife–AR husband mating, so that the frequency of AB × AR, disregarding the sex of each parent, amounts to 2·2 per cent. of all matings.

Now it is known what children, in what proportions, result from each mating. Thus, given the group of the child, we can calculate the relative chance that it resulted from each of the possible matings. And in each possible case it is known whether one or both of its parents is of compatible group, and hence the chance that "a parent" is compatible.

To give an instance, suppose that the patient is of Group IV., represented by RR. An RR patient may be the child of any one of six matings. Column (*a*) of Table IV. shows these matings, and column (*b*) the frequency of each, as a percentage of all matings. Column (*c*) gives the proportion of children of each mating who are RR. Column (*d*), given by (*b*) × (*c*), thus gives a measure of the relative chance that the RR patient is a child of each mating. Clearly a mating, all of whose offspring are RR, is a more likely parentage for the RR patient than an equally frequent mating, of which only a quarter of the children are RR. Column (*e*) expresses this chance of each origin as a percentage.

Column (*f*) now states the proportion of the parents who are RR and hence compatible, and (*g*), given by (*e*) × (*f*), is the final probability that a parent will be compatible.

TABLE IV

(*a*) Mating.	(*b*) Frequency of mating.	(*c*) Proportion of children RR.	(*d*) Relative chance.	(*e*) Absolute chance.	(*f*) Proportion of parents RR.	(*g*) Chance of compatible parent.
	Per cent.		Per cent.	Per cent.		Per cent.
1. RR × RR	21·5	1	21·5	46·5	1	46·5
2. RR × AR	33·6	½	16·8	36·5	½	18·2
3. RR × BR	6·4	½	3·2	6·9	½	3·5
4. BR × AR	5·0	¼	1·2	2·6	0	0
5. AR × AR	13·1	¼	3·3	7·2	0	0
6. BR × BR	0·5	¼	0·1	0·2	0	0
—	—	—	46·1	99·9	—	68·2

Thus "a parent" will be compatible with a Group IV. patient in 68 per cent. of cases. It should be noticed that this is not the same as the chance that "one or other" parent is compatible, which is obviously greater, since, if the first parent is incompatible, there is still a chance that the second may be compatible. Thus in this case it is seen from Column (*a*) that in rows 1, 2, and 3 *one of the two* parents is RR, the corresponding factor in Column (*f*) becoming 1 for these, and the total now becoming 90 per cent.

The calculation for the composite Groups II. and III. is performed in a manner similar to that used before for children. Thus the probabilities are obtained for AA and AR separately, and then averaged appropriately.

Further, it is clear that the probability of a brother or sister proving compatible is readily obtained by almost the same method as for parents. Instead of inquiring what proportion of the two parents is compatible in each "family," we inquire what proportion of the (other) children is compatible. It is to be noted that the chance of occurrence of any particular assortment of genes is unaffected by which assortments have already occurred in the family; just as the chance of a penny falling "heads" depends only on the details of the toss, and not on the results of previous tosses.

Thus in the case of an RR patient, the analysis is the same as in Table IV. until column (*e*), after which it is as Table V.

In this way all the probabilities in Tables I. and II. can be obtained. It is true that in any one family, the proportion of children of the various groups will not be exactly, or even approximately, according to theoretical expectations. If the assumptions underlying the calculation are true however, the probabilities would be confirmed by taking a large enough number of cases, and are thus the correct expectations in each particular case.

TABLE V

(*a*) Mating.	Children.	(*c*)	(*b*) Proportion of RR children.	(*i*) Probability of compatible brother or sister.
		Per cent.		Per cent.
1. RR × RR	RR	46·5	1	46·5
2. RR × AR	RR AR	36·5	½	18·2
3. RR × BR	RR BR	6·9	½	3·5
4. AR × BR	AB AR BR RR	2·6	¼	0·6
5. AR × AR	AA 2AR RR	7·2	¼	1·8
6. BR × BR	BB 2BR RR	0·2	¼	0·0
—	—	—	—	70·6

In the case of unrelated persons, these probabilities may legitimately be combined. Thus, if the chance that such a person should be of different group from a patient is 10 per cent., the chance that three such persons should all be of different group from the patient is (10 per cent.) = 0·1 per cent. The same argument cannot however be applied to relatives. Thus, if an RR patient has an incompatible brother, they cannot be the children of an RR × RR mating, which gives only RR children; and for the remaining possible families the chances of a compatible brother are not so favourable and the expectation for the next brother tested must be revised accordingly. If, on the other hand, a parent has been found to be incompatible, certain families are ruled out, but in the remainder the second parent is certain to be compatible, except in the few cases in which a child is incompatible with both parents. The chance of compatibility for the second parent may thus prove to be greater.

TABLE VI

Chance of Compatibility of Second Relative

	Parent.	Brother or sister.	Child.
BLOOD TO BE OF PATIENT'S OWN GROUP			
Donor:	72 per cent.	46 per cent.	40 per cent.
BLOOD TO BE OF ANY COMPATIBLE GROUP			
Donor:	72 per cent.	44 per cent.	36 per cent.

Table VI. gives the chances (weighted average for all groups) for a second relative of each kind to be compatible, a first relative *of that kind* having proved incompatible.

CONCLUSIONS (SEE TABLES I AND II)

1. Of the near relatives, a brother or a sister is the most likely to prove compatible as a donor, but the advantage is negligible except in the case of a Group I. patient requiring a transfusion of blood of the same group.

2. When blood of the patient's own group is required, the advantage of relatives over unrelated persons is large, especially in the rarer groups, I. and III. Two unrelated persons are equivalent to one relative in chance of providing a donor. A relative is twice as likely to be compatible as not.

3. When blood of any compatible group is sufficient, the advantage of the relative is less. "One and a half unrelated persons" are equivalent to one relative. A relative is four times as likely to be compatible as not, whereas an unrelated person is twice as likely to be compatible as not.

4. It is also found that if one parent has proved to be incompatible, the other parent has a nearly equal chance of proving compatible (Table VI.). If, however, one child has proved to be incompatible, any further child has a decreased chance of proving compatible, and the same applies for brothers and sisters. In fact, when blood of any compatible group is sufficient, if one son (or brother)

has already proved incompatible, an unrelated person is much more likely to be compatible (67 per cent. as against 40 per cent.) than another son (or brother).

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MEDICINE AND THE LAW

Medical Certificate Signed by Unregistered Practitioner

William Mellor, of East Dulwich-road, East Dulwich, was fined £10 and 20 guineas costs on Jan. 6th at Lambeth police-court for offences against Section 40 of the Medical Act. One summons charged him with wilfully and falsely using the title of "Doctor of Medicine," the other with wilfully and falsely using the description of "medical examiner," thereby implying that he was a registered practitioner. The defendant's name was not, and never had been, on the Medical Register. The offences were of some public importance since they arose in respect of a medical certificate given to an applicant for an air pilot's licence. The Air Ministry requires a medical examination in such cases in order that the medical fitness of the applicant may be assessed. A number of questions must be put by the medical examiner who must enter various particulars on a form. The form is headed by a preliminary note stating that the medical examiner must be a registered medical practitioner with British qualifications. Mellor signed in the space prescribed on the form for the signature of the medical examiner: he added his qualifications as "M.A., M.D., B.Sc., Lic. Hom. Med. (Ind.)." It was the "M.D." in this list which got him into trouble. In effect also he had put himself forward as a medical examiner who possessed the required British qualifications. In the witness-box he stated that, when he signed the prospective pilot's application form, he had not noticed the printed words "Medical Adviser." This abstraction of mind the court was evidently unable to accept. Mellor produced several framed certificates and diplomas; he said he held four degrees obtained after examinations conducted in London and Liverpool under extension arrangements with a university at Kapurthala in India and other institutions in America. It is possible that the Air Ministry officials had their suspicions aroused by the over-simplification of the entries made by Mellor. Against "visual acuity," for instance, he had written "v. good" without filling in the details which the form required.

A third summons related to the name-plate exhibited on the railings outside the defendant's address. It contained the description "Dr. Wm. Mellor (India), Homœopath and Osteopath, U.S.A." This became the basis of a charge of having wilfully and falsely used the description of doctor, thereby implying that he was registered under the Medical Act. The magistrate dismissed this third summons, being presumably not satisfied that Mellor had "wilfully and falsely" misdescribed himself in view of the evidence of Indian and American qualifications which the prosecution was hardly in a position to disprove. The serious element in the case was the pretence of being a registered medical practitioner for the purpose of the medical certificate of an applicant's physical fitness to pilot an aeroplane. The Medical Defence Union does good service to the public as well as to the medical profession in undertaking proceedings of this kind. It is seldom an easy matter to obtain convictions under Section 40, where the statutory expression "wilfully and falsely" introduces technical difficulties. It is not unreasonable to assume that unregistered practitioners would usually like to be taken for registered practitioners. Occasionally, it is true, an unregistered man, when charged under Section 40 of the Act, protests that nothing was further from his thoughts than to pretend to be a fully qualified doctor. If so, as Lord Hewart hinted not long ago in the High Court, there are plenty of ways by which the unqualified man can differentiate himself in the description he adopts. To call himself "doctor" is not one of them.

SCOTLAND

(FROM OUR OWN CORRESPONDENT)

EDINBURGH ROYAL INFIRMARY

THE annual report of the Edinburgh Royal Infirmary for 1936 gives interesting figures of advance during the past year. There were 21,568 in-patients, and of the 20,612 whose treatment had been concluded, 5536 were medical cases and 15,076 surgical. On an average there were 965·52 patients a day (including 72 children) with a length of stay of 17·14 days (on the medical side 26·04 days, and on the surgical 13·87). The death-rate was 6·2 per cent., or, after deducting deaths within 48 hours, 4·3 per cent. Operations in the in-patient theatres amounted to 11,682. There were 72,543 new out-patient cases admitted, with 379,688 attendances. Motor accidents accounted for 415 admissions to the wards—an increase of 49 over the previous year—and 587 to the out-patient department. Legally, the Infirmary could claim compensation for the cost of maintaining these cases, but in practice it was found that the amount received did not cover half the cost involved. The managers of the hospital regretted that it had not been possible to effect any reduction in the waiting-list.

The work on the new maternity pavilion and nurses' home has been delayed by bad weather during the winter months, but it is hoped that these buildings will be ready for occupation by the end of 1937. Accommodation for sick nurses is being added to the new home at an extra cost of £6700. The full building scheme will cost about £500,000, of which some £300,000 has been contributed, and the managers propose shortly to make an appeal to the public for the additional £200,000. Important and far-reaching alterations are being carried out in the X ray department; new apparatus is being provided, including a very powerful tube primarily for the treatment of cancer, while the staff has been considerably increased.

A cause of concern to the managers has been the growth in expenditure, amounting to £40,000 in ten years, and they earnestly appeal for new and greater subscriptions. The total ordinary expenditure amounted to £169,694, an increase over the preceding year of £12,996, and the net result of the year's work showed a deficiency of £77,006. Fortunately, the sums for general purposes received by legacies and special donations amounted to £78,659, and it has thus been possible to meet all outgoings without drawing on invested income. A gratifying feature has been an increase of £3759 in the amount received from the League of Subscribers. The system of

budgeting adopted a few years ago enables a strict control to be kept on all outgoings, but extraordinary expenditure, owing to works of reconstruction and alteration, has again been high, amounting to over £28,000.

A NEW NURSES' HOME IN GLASGOW

A scheme that will be a notable "city improvement," by adding to the open spaces near the Cathedral and by greatly contributing to the beauty of Cathedral-square, was referred to at the annual New Year's meeting of the managers of Glasgow Royal Infirmary with the nursing staff. The new nurses' home, the design for which has now appeared in the public press, is to be erected at a cost of £100,000. Tenements belonging to the Royal Infirmary and to the corporation are to be demolished, while it is hoped that the small Cathedral Hall may be transferred to another site. The only building then left, besides the home, would be Provands Lordship, the oldest house in Glasgow. The new home is to be H-shaped in design, consisting of a centre block and wings, with the ground between the wings laid out with lawns and flower beds. The frontages will extend to 200 feet, with side frontages of 128 feet. All the bedrooms will be single and supplied with hot and cold water, while there will be ample accommodation for recreation, writing, reading, study, and work rooms. Automatic electric lifts will give access to all floors. The construction is to be partly of light cream polished sandstone and partly of purple-grey brick.

PANEL AND CONTRACT PRACTICE

The District Medical Service

A SERVICE which affects some 3000 practitioners, and in some areas a not inconsiderable section of the population, is obviously of importance to the profession and the public. Though the appointment of a "district medical officer" under this specific designation dates from 1847, arrangements for medical attendance on the poor prevailed generally before this period. Previously to the Poor Law Act of 1834 provision rested with the overseers of each parish who contracted with a local practitioner; the method has its relic in the term "parish doctor" still occasionally used. Under the 1834 Act the duty passed to the newly constituted boards of guardians, who were urged by the Poor Law Commissioners to take into early consideration the appointment of medical officers. The effect of legislation has been towards a centralisation of control, further manifested by the Local Government Act, 1929; thus, before 1834 responsibility rested with 15,000 parish officers, and in 1929 the responsibility was transferred from 609 boards of guardians in England to the 132 councils of county boroughs and county councils.

A century ago the service seems to have been very extensive in scope and to have provided the usual form of medical attendance on a large section of the wage-earning population. It was also more of a rural problem than it is to-day, though the practice, probably continuous with former times, may still prevail under which an agricultural labourer with a large family is regarded as entitled to medical relief. Increasing urbanisation has moved the centre of interest to the towns, and in recent years the unfortunate effect of prolonged unemployment has, especially in certain areas, largely increased the numbers of those compelled to seek medical relief. This variation may be illustrated by the following figures which show the number of persons (on Sept. 26th, 1936) per 10,000 population in receipt of poor relief—an approximate index of medical relief:

Counties		County Boroughs	
Bedford	99	Coventry	116
Wilts	150	Brighton	187
Durham	717	Newcastle-upon-Tyne	687
Glamorgan ..	682	Liverpool	1068

No uniform method of providing medical attendance has prevailed. The most usual method has been the appointment of local practitioners on a part-time salary basis, and the majority of medical relief districts are thus officered to-day. In the earlier years after 1834 the appointment was frequently put up to tender, a practice which was obviously undesirable and which came to be discountenanced by the Poor Law Commissioners. Salaries were fixed at the discretion of individual boards of guardians, and consequently show considerable variation throughout the country. In some rural districts remuneration may have remained unaltered with a dwindling population; in urban districts, on the other hand, especially in those with a heavy incidence of unemployment, there may have been altogether insufficient adaptation to the increased demands. Some authorities have latterly devised methods of correlating payment to work done. The system is too well known to require elaboration; the officer appointed carries out his duties in the ordinary routine of general practice.

Less frequent has been the appointment of whole-time officers. The first such appointment was in operation at Leighton Buzzard in 1840, but the system has not been extensively followed. Such officers may devote the whole of their time to district medical duties, combined perhaps with those of public vaccinator, a method which prevails for instance in parts of Birmingham and West Ham, in Smethwick and Middlesbrough; the major part of the work is done at central dispensaries, usually attached to relief stations. A criticism made of such service is its obvious relation to the Poor Law.

Whole-time officers, again, may combine the duties of district medical officer with other functions such as the charge of a public assistance institution or an appropriated hospital, thus providing a wider range of interest and a linking up of in-patient and out-patient treatment. In several districts of London the duties of district medical officer are carried out by the resident staff of L.C.C. hospitals. Again, but very exceptionally, the duties may be combined with those of medical officer of health to one or more district councils.

THE FREE CHOICE SYSTEM

These have until recent years been the customary methods by which the work has been conducted. Since the introduction of the Local Government Act, 1929, this service has, with other functions transferred from boards of guardians, come under review by the local authorities concerned, but it remains a poor-law function as there exist no powers under the Public Health Acts for the provision of a domiciliary medical service. While the majority of authorities have continued on former lines, with perhaps some adjustments, others have introduced what is known as the "free choice system" whereby

the work is thrown open to a panel of practitioners willing to act. The idea is not new; it was suggested in a memorandum submitted by the British Medical Association to the Poor Law Commissioners in 1839, and has been in operation in a small area in Kent since 1928. Its re-emergence as a policy is due primarily to the view that it would tend to minimise the association of the service with the Poor Law and it has been stimulated by the former lapse from medical benefit of many insured persons and the consequent resort of these and their families to the poor-law provision, usually involving a change of medical attendant.

The system cannot be put into immediate and full operation in any area, for district medical officers have security of tenure, so that there can only be partial introduction as existing appointments fall vacant. It was first introduced in Newcastle-upon-Tyne in 1933, and in the same year was adopted in Wiltshire and East Ham; in 1935 it applied to 7 out of 10 medical relief districts in Newcastle-upon-Tyne, to 18 out of 68 in Wiltshire, in East Ham to the whole borough except one small district. Introduction to a varying extent has since taken place elsewhere as, for example, Warrington county borough, and the counties of Cambridge, Cornwall, East Suffolk, Essex, and Glamorgan. The general operation of the system is much the same in all areas but there is considerable diversity in remuneration. Thus, in Newcastle the payment is 5*s*. per patient-quarter for short-period cases, and £1 a year for those under treatment for more than two consecutive quarters; in East Ham the rate is 16*s*. per patient-year; in Wiltshire it is 25*s*. for each case seen during the calendar year (20*s*. in one district), and here the payment covers the supply of drugs. The service provides a patient with the doctor of his choice, and is thus in line with private practice and with medical benefit under the National Health Insurance Acts. It is likely to be more costly than the other methods mentioned, which however have not infrequently been underpaid. Its possible reaction on public assistance will be scrutinised by administrators. It introduces the local authorities to a closer contact with the general body of practitioners in their areas, and this may prove a prelude to further developments.

Dr. J. A. Charles has reported [1] on the working of the system in Newcastle; it would be well if similar comprehensive reports were provided from other areas where the system has been in operation for a sufficient period so that fuller details of its working may be available for the guidance of others. No medical service can in these days remain static, and this latest development in the district medical service will be watched with interest in its relation to the sick person, the medical profession, and public administration.

Capitation Fee for Adolescents

As we set out a fortnight ago the Ministry of Health and the Insurance Acts Committee failed to agree about the terms on which medical benefit shall be provided for young people between leaving school and reaching insurable age. The I.A.C. decided to consult representatives of local medical and panel committees about the impasse thus created and a conference was held on Jan. 7th in the Great Hall at B.M.A. House with Dr. D. Elliot Dickson, of Lochgelly, Fife, in the chair. Despite the prevailing epidemic a fully representative gathering was secured, although the list of deputies was long. The report of the I.A.C. having been moved by Dr. H. C. Jonas, the conference agreed, at the suggestion of Hastings, to the discussion being conducted in private. At the conclusion it was announced that the following resolutions had been passed without dissent.

That the offer of the Minister of Health of a capitation fee of 7*s*. 6*d*. for medical attendance on insured persons under 16 years of age be rejected.

That in view of the inadequacy of the existing capitation fee, and pending the result of negotiations for its increase, this conference is not prepared to accept for attendance on insured workers under 16 years of age a capitation fee less than that paid for adult insured workers.

That this conference recommends insurance practitioners to decline service for the provision of medical benefit for insured workers under 16 years of age on the terms offered by the Minister of Health.

That the I.A.C. be authorised to take action in the light of the decisions reached by the conference.

NON-MEDICAL COMMENT

In an article entitled Views of the Doctors the *National Insurance Gazette* sets out fully the case made by the I.A.C., quoting almost verbatim the general statement of that committee's views summarised in our columns a fortnight ago. The *Gazette* itself sees no difficulty about either of the questions outstanding between the I.A.C. and the Ministry. The doctors "have complained, more or less bitterly," the *Gazette* remarks, "of the amount of clerical work thrown upon them—all of it distasteful to professional men who could spend their time in much better ways other than doing mere clerk's work. . . . The only point is that the doctors cannot be allowed to say that it is a big thing when they want paying for it, and nothing when they have to give it up." On the second point—are adolescents in need of the same amount of medical attention as the existing insured population?—the *Gazette* suggests that the reply "must be based mainly on medical and statistical knowledge"; concluding, "We are interested in a fair settlement for two reasons. As citizens and taxpayers we want the State to get a square deal: as National Health Insurance workers we want the benefit to the school-leavers to be satisfactory."

Retirement of Sir Walter Kinnear

The retirement, on Jan. 1st, of Sir Walter Kinnear from the position of controller of the Insurance Department of the Ministry of Health, which he had held since 1919, deprives the public service of one of its most distinguished and popular members. As a student at the Royal University of Ireland, he had a brilliant career, graduating with honours in mental and moral science, and soon became a prominent figure in the insurance world. In 1911 he was appointed deputy chairman of the Irish National Health Insurance Commission, and during the later years of the war he was seconded to the English Commission. His success in handling the difficult problems that beset the inception of the health insurance system both in Ireland and in England clearly showed that he would be in his right place as head of the Insurance Department of the newly constituted Ministry of Health. He was not only a highly efficient and popular administrator, with the personal charm characteristic of many of his countrymen, but his thorough grasp of the principles of insurance in all their bearings made him an international authority on the subject. His voice was influential at Geneva, and last year, by special request, his services were made available to the Australian Government to assist in exploring the possibilities of national insurance in Australia. He carries with him into retirement the good wishes of all who were associated with him in his long and distinguished career.

[1] *Lancet*, 1936, **2**, 1361.

GRAINS AND SCRUPLES

Under this heading appear week by week the unfettered thoughts of doctors in various occupations. Each contributor is responsible for the section for a month; his name can be seen later in the half-yearly index.

FROM A PUBLIC HEALTH CLINICIAN

III

THIS is coronation year and different coronation thoughts pass through our minds—to nearly all a procession is one of the foremost. If we personally do not want to see the procession it is certain that some members of our family will so wish. Granted the time, I should like to see the coronation procession if that were all, but there will be crowds and crowds and a very early start will be necessary; unluckily it is not possible to take a seat at 11.25 for an 11.30 procession and then leave quietly. Everyone in their lifetime should see one great procession—mine was the funeral procession of King Edward VII. The night before I had spent over 4 hours in a queue to see the lying in state at Westminster Hall and then came away disappointed. Fortunately the crowd was not, as the papers declared, "pervaded by a spirit of silent reverence," and there were many humorous incidents, but it was tiring for all that, and left me determined never again to queue up for anything. So next day I arose late and set off to see the procession. Walking in mid-road along the route the vastness of the crowds impressed me. Now and again I sidled one way or the other to secure a stance, but a chorus of protests moved me on. Suddenly it struck me that when the procession passed the side roads would be closed, so I took up a humble position at the back of the crowd, at a point where a side road entered, confident that, when that road was closed, I should be propelled willy-nilly into a front place; and so indeed it befell.

Passing through life one has at times similarly useful inspirations, or experience suggests something that has not yet occurred to others; at the large cheap restaurants where I take my meals I have noticed that small waitresses are usually the quickest, an observation that has proved time saving. Another similar discovery was that if when waiting, and waiting, to be served in a crowded room I sat back and obviously read a large evening paper steps were soon taken to secure service. It would be interesting if others would give us the advantage of similar discoveries among the smaller things of life.

* * *

Most practitioners can narrate experiences outside the routine of normal medical practice. Thirty years ago, when acting as locum in a Hampshire practice, I had as temporary partner a wise and observant practitioner. Called one day to see a blind woman in later middle age, the patient told me that during the night her husband, dead some 10 years, had visited her, stood at the foot of the bed and conversed pleasantly. She had been blind for some 15 years, but averred that on this occasion she had seen her husband as clearly as she had ever seen in her best years. During the afternoon I told my partner the story, and he remarked, "She'll be dead before to-morrow." I asked why? The patient was ailing, but there was nothing to justify such a prognosis. "They always die when they tell those stories" was his reply.

Since then my experience has confirmed that practitioner's belief. An old lady, 10 years a widow, told me her husband had visited her and she saw him "more clearly than I see you now," though she had never seen him since death, and was not at the time thinking of him. Within 12 hours that patient had died also, and it has happened similarly with 2 other patients. It is not only husbands or wives that are seen, but any intimate friend or relative who is no longer alive.

Speaking to a clergyman, with a far more intimate experience of dying folk than I am ever likely to acquire, he told me of several similar instances he had met with and believed that if the patient was sufficiently conscious to describe it such an experience would be found to be usual. As this is not a theological lecture I will pass over the explanations he offered; for myself I have no explanation and am left wondering. My own experience of such events is too limited for any generalisation, errors of observation or narration may have crept in. I wonder.

* * *

Ornithology is rather a favourite pastime for doctors with botany a close second. We are speaking of course of the active-minded members of the profession, or would it not be more correct to say natural history minded; for many, if not the majority, who find an alternative solace in bridge or golf have equally active minds. The study of bryology and mycology, meaning by that mosses and fungi, is less popular and yet equal in interest to botany. The mosses are difficult because a proper study entails low-power microscopy, but if the observer remains a dilettante, as previously advised, and intelligent recreation is his chief objective, resort to the microscope will be seldom needed. For fungi a pocket lens should suffice, but this form of life presents a field quite equal to that of botany. My first discovery of *Clathrus cancellatus*, a large fungus showing a wide grey network with large mesh, was indeed a red letter day; and then there are various stag-horn and stink-horn fungi, some of them bearing ancient and almost lewd latin names. It is interesting also to note the varied forms of parasitism displayed, and how the death of trees and other vegetation is caused. The ways of nature are indeed ruthless.

The difficulties of the fungus hunter are that wet weather is always best and may be essential for certain forms, and that many fungi have a distinct smell, sometimes a most offensive distinction. My children, trained in natural history methods, will stop suddenly when passing through a wood and call out "stink-horn somewhere near." And there are others almost as bad as the stink-horn. The hunt for fungi is called for some reason a foray, though I know not why, akin perhaps to the special names—flocks, droves, coveys—of groups of various animals, or to names given to different nests, as earth, dray, or holt. I should like to see more doctors interested in fungi.

* * *

Apart from natural history, history itself provides a fascinating if more sedentary hobby. Gibbon's

"Decline and Fall" presents useful pabulum for a train journey, far better than most novels provided always that the reader has not already read it, as so many have done, when too young fully to appreciate the charm. I read Gibbon's "Decline and Fall" for the first time in trains, and it took quite a long time. I am now engaged on Grote's "History of Greece" which has not quite the same attractions and will take longer, in fact it seems possible that when death overtakes me, Grote's History will still be unfinished.

The secret of enjoyment of such reading is never to read for instruction, never to regard the reading as a lesson, never to attempt to remember, but to read purely for amusement and recreation. Novels and films show us life as it might be but certainly is not, history presents life as it was and still very much is. Gibbon is not the only work commended; there are English histories, French histories, and period histories. Then a similar field is covered by biographies which may give an interesting high-power view of some special time or place.

A knowledge of human nature is of the highest importance to any doctor, and his life's work presents constant opportunities for expanding his knowledge, but to know human nature one lifetime is not enough; history may assist.

* * *

Archæology attracts many devotees; it used to attract me and many pilgrimages have I made to old buildings and well-known churches, but to-day the taste has passed, as tastes will sometimes, possibly the result of too many archæological excursions. The study has its limitations and has not the attraction of natural history, but it is interesting to form conceptions of the habits and life of our ancestors disclosed by a study of their buildings and remains.

The past deserves respect and may provide lessons and examples useful to-day, but if the sixteenth century had been solely devoted to the past we should have missed many of the renaissance productions which receive homage to-day, and should still be admiring rush-covered floors and the rather clumsy architecture of the Dark Ages. Perhaps teamwork here, as in medicine, is best. Those who feel so impelled will produce for us new forms of art and architecture while the archæologists criticise these from their knowledge of the past.

CORRESPONDENCE

INFECTION AND DISINFECTION

To the Editor of THE LANCET

SIR,—The lecture by Sir Weldon Dalrymple-Champneys reproduced in your issue of Jan. 9th will be read with interest by practitioners other than medical officers of health and should appeal to the educated layman. I should like to refer to three points.

First, whooping-cough. If it is true that the patient has already ceased to be infectious *by the time the "whoop" appears*, then many young prisoners may be liberated safely and much domestic inconvenience ended. We all know that the whoop may persist long after infection has disappeared, but experience (apparently fallacious) has suggested that the early convalescent may be a source of infection. Moreover, if this be correct, our present efforts at prevention are futile.

The inclusion of infectious disease blocks in general hospitals is not peculiar to Scandinavia. It has long been the practice in our naval hospitals without, so far as I know, any untoward results. Doubtless it would have been adopted more widely were it not for the fact that local authorities provide for infectious disease and, for the most part, voluntary bodies for other sickness. Nevertheless the idea is valuable on the grounds that small isolation hospitals are usually uneconomical and inefficient, and that unduly long journeys are not in the interest of the patient even under modern transport conditions.

Lastly current and terminal disinfection. There is no doubt that "a good spring cleaning" is all that is necessary in most diseases when the patient has been treated at home throughout his illness, but I suggest that the full ritual is desirable in the case of diphtheria patients removed to hospital while still highly infectious, and when any infectious disease occurs in a boarding house or hotel. In scarlet fever practice varies. Admitting that infection in this disease is mainly *personal* to the sufferer, undetected cases and carriers, there still remains sufficient evidence in the opinion of many to justify full disinfection.

I am, Sir, yours faithfully,

G. B. PAGE,
Medical Officer of Health, Exeter.
Public Health Department, Exeter, Jan. 11th.

NASAL SINUSITIS IN CHILDHOOD

To the Editor of THE LANCET

SIR,—Your leader on this subject draws attention to a common malady but one not very familiar to those in charge of young children and school-children, judging from the regular stream of cases referred to hospital for removal of tonsils and adenoids, when the underlying condition is a nasal sinusitis.

Complete nasal obstruction in infants and children is most commonly associated with a nasal discharge due to a sinusitis, which is also a fertile cause of a recurrent otitis, chronic cough, and relapsing chest conditions. A large mass of adenoids produces only *intermittent* nasal obstruction. In my experience the mucoid nasal discharge arises more frequently from the ethmoidal cells than from the antra.

Cases of nasal sinusitis may often be recognised by the presence of nodules of lymphoid tissue scattered on the posterior pharyngeal wall, visible below the level of the uvula. A blob of mucus depends from the post-nasal space, coming into view when the child gags. In the presence of these signs, a cure of the nasal symptoms cannot be obtained by removal of tonsils and adenoids. The incidence of "clinical" nasal sinusitis is certainly more common than is realised, but percentages are deceptive. Anyone interested in the subject—especially if he is known to have some "new" treatment—soon becomes inundated with cases that are referred from all quarters, with the result that an exaggerated idea is obtained as to its real prevalence.

In the last five years at the Queen's Hospital for Children I have made it a routine to wash out the antra in all cases with a nasal discharge. I can only recollect some half a dozen cases in which pus was washed out of the antrum. (I exclude cases of

complications such as orbital cellulitis secondary to an acute pan-sinusitis.)

Most of the antra must have contained only watery mucus, or have been empty, as the wash-outs were returned clear, in spite of the X ray disclosing antra which were completely opaque. This opacity must therefore indicate a thickened lining membrane only. I have never observed a fluid level in the antra of children. On a few occasions in the past, on clinical and radiological grounds, I have explored the antrum through the canine fossa, and have been disappointed by the small amount of disease disclosed—merely a slight thickening of the mucous lining of the antrum with no fluid visible. The discharge must therefore have had its origin in the ethmoidal region.

A difficult problem arises in considering the treatment of the chronic cases—and many become so in spite of all types of treatment.

All my patients are treated as a routine with a course of nasal lavage and displacement, which is performed as follows. The child lies down with the head well extended over the edge of the pillow, so that a line through the tip of the nose and the auditory meatus is vertical. While the child chants "K," "K" continuously, a solution of normal saline (with ½ grain of ephedrine hydrochloride added to ½ pint) is slowly dropped from a rubber bulb syringe into one nostril, while a nozzle attached to a suction apparatus applied to the other nostril draws the fluid away. In this way the nasal chambers are thoroughly flushed with the solution, and all adherent and tenacious secretions removed. The ephedrine shrinks up the nasal mucosa and facilitates drainage from all the sinuses. The symptomatic relief is instantaneous and impressive. About 4–6 oz. of solution is used for each nostril. The treatment is repeated 2–3 times weekly for six weeks. At the end of each seance, 20 c.cm. of solution are dropped into the nose slowly. One nostril is blocked with the finger, while intermittent suction is applied through the other nostril—to "displace" the solution into the sinuses. The child's coöperation is essential. I have used this treatment for the last four years and the results on the whole have been gratifying in the acute and subacute cases. The chronic cases derive considerable benefit, but tend to relapse when the treatment ceases.

If the symptoms are not relieved, antral lavage is practised under anæsthesia and the nasal displacement repeated subsequently. I have been disappointed with the results of antral drainage, and only after much consideration do I perform an inferior intranasal antrostomy, as I consider many of these cases to be ethmoidal and not antral in origin.

I am, Sir, yours faithfully,

London, W., Jan. 7th. N. ASHERSON.

PURIFIED LIVER EXTRACTS

To the Editor of THE LANCET

SIR,—In your issue of Dec. 26th last Dr. C. C. Ungley describes the trial in pernicious anæmia of a preparation said to be a "further purification of Dakin and West's liver fraction." He states that the further purification has been obtained by applying the process described by us in the *Acta Medica Scandinavica*. The method described in his article, however, as used for this "further purification" consisted in applying only one part of our method to anahæmin, the original Dakin and West liver fraction.

In terms of the still unisolated anti-anæmic "pure factor," the product examined by Dr. Ungley must be a relatively crude one. By our method of adsorption on charcoal and selective elution with phenol-water and phenol we have consistently prepared direct from liver active material in very high concentration. In terms of the "total solids" present, the potency is considerably higher than that of Dr. Ungley's preparation. We maintain, however, that a mere statement of the total solid content of a liver extract is, in the present state of our knowledge, likely to be very misleading; in our opinion, writing as chemists, it may involve clinicians in serious fallacies.

Our investigations indicate that the Dakin and West method leads to inconsistent results and that it also involves a considerable loss of the anti-anæmic factor. By adsorption on charcoal and selective elution with phenol-solutions we obtained active material at a high concentration; we also found that our process gave rise to a product of remarkably constant clinical activity. By repeating the process of adsorption and elution, followed by other methods of purification not yet published in detail, further concentration of the hæmopoietic factor could be obtained. This is shown by the fact that we prepared material of such potency that 0·7 mg. produced a high reticulocyte response in the hands of Strandell, Poulsson, and Schartum-Hansen.

We wish, however, to insist that even after this degree of purification we had not obtained the chemically pure factor. It is probable that at least two-thirds of our richest material consisted of inert matter.

At the present time, therefore, we consider it is undesirable to state the dosage of a parenteral liver extract in terms of total solids, since inert substances must constitute a large proportion of the product, unless we push the purification to an advanced and uneconomical stage. If we assume that the amount of pure factor in a dose weighs 0·5 mg. (which is likely to be much too high) the statement that "25 mg. of solids gave a maximal response" shows the dose to contain 98 per cent. of inert matter and 2 per cent. of the active factor. We agree, of course, that a low total solid content is desirable, but not that this gives a standard by which we can estimate dosage. We can produce from a given quantity of fresh liver a product of *unvarying* potency with a *very low* total solid content by stopping our process at a given stage, but the actual weight of the dose may vary by 50 or even 100 per cent.

On the manufacturing scale, the proper objective must be to produce in the highest practicable degree of purity an anti-anæmic preparation of unvarying potency. Dr. Lester Smith, of the Glaxo Laboratories, Greenford, England, working in conjunction with us, has now been able by this method to make such a preparation, in which is produced from 100 grammes of fresh liver a fraction having an average weight of about 10 mg. The material is dissolved in 2 c.cm.—i.e., at a concentration of about 5 mg. per c.cm. A maximal reticulocyte response occurs after the injection of a quantity of material produced from 100 g., or at the most 200 g., of fresh liver, with a corresponding rise in the red blood corpuscles. This product, as is clear from its small weight, is of a high degree of concentration, but it is our earnest hope that the dose will not be stated in terms of its weight. At the present time we rely upon the standardised method of manufacture and the constant potency that has been found clinically. Expression of activity in terms of the weight of original fresh liver has a useful meaning only in such an instance.

We understand that clinical trials of this product are being made in England (as well as in this country) and that it will be generally available before long. We must apologise for trespassing on your space at such length, but we think it only fair to ourselves and our English collaborators to make it clear that the paper by Dr. Ungley, except for the one step in purification described, has little reference to our own published work or to our more recent investigations.

We are, Sir, yours faithfully,

PER LALAND,
AAGE KLEM.

Oslo, Norway, Jan. 6th.

CONVALESCENT SERUM IN INFLUENZA

To the Editor of THE LANCET

SIR,—On analogy with other virus diseases, such as measles, it seems reasonable to assume that serum obtained from patients convalescent from influenzal might be of therapeutic benefit. The suggestion was, we believe, first put forward by Dr. Herbert French in 1919, but has never been practised, at any rate on a large scale. The recent researches of Laidlaw on the transmission of influenza to ferrets have shown that these creatures do in fact develop antibodies as the result of an attack. This would be a strong point in favour of the use of convalescent serum were it not that after a few months of immunity they become again susceptible, even though antibodies are still in the blood. Possibly, however, protection depends in part upon these substances, and upon their degree of concentration in the body.

Our purpose in writing this letter is to ask those medical men who are now dealing with influenzal patients to obtain blood from them when they are convalescent. If they will send either the blood or preferably the patient to the Bacteriological Department, Guy's Hospital, a batch of mixed sera will be obtained and treatment of influenzal patients carried out with the usual controls. It is hoped in this way to decide whether the serum is of any value and, if so, to aim at the collection of large supplies so that we may at last have some substance of definite therapeutic and prophylactic value to guard the population against future epidemics. Will those doctors who are good enough to collaborate in this manner kindly select only those patients in whom the diagnosis of influenza was unquestionable and preferably uncomplicated?

Blood may be collected into a sterilised vessel by any of the recognised aseptic methods of venepuncture, and the following suggestions for the collection of serum may be helpful:—

If apparatus is not to hand, on receipt of a message to Hop 1654 collecting apparatus will be sent to any medical man offering to send blood. This will consist of a sterilised needle and rubber connexion fitted to a sterilised 250 c.cm. screw-capped bottle. The skin over an arm vein should be carefully cleaned, the vein distended by pressure higher up the arm and venepuncture performed in the ordinary way, the blood being run directly into the bottle. When this is nearly full, the pressure on the arm is released, the needle withdrawn, a pad placed on the site of puncture and the cap screwed on to the bottle. The blood should then be sent directly to this department. The whole procedure must be as aseptic as possible. If the patient is sent to the laboratory for blood collection, a preliminary telephone message would be appreciated.

We are, Sir, yours faithfully,

A. H. DOUTHWAITE,
F. A. KNOTT.

The Bacteriological Dept., Guy's Hospital, S.E.1, Jan. 11th.

BUFFER ACTION IN GASTRIC DISORDERS

To the Editor of THE LANCET

SIR,—We would like to draw the attention of English colleagues to some observations we have made on the utilisation of buffers in the treatment of gastric disorders.[1]

The optimum acidity for peptic digestion ranges from *p*H 1·5 to about *p*H 4·0; below 1·5 the stomach is liable to be attacked by its own contents, and above 4·0 pepsin ceases to act. From this it may be supposed that disorders due to irregular acidity of the gastric juice will be relieved by a remedy that maintains a hydrogen-ion concentration near the optimum. Such a remedy, unlike the acids and alkalis usually employed, should be capable of correcting both excessive acidity and excessive alkalinity. This property is possessed by the substances called buffers, which are usually mixtures of at least one salt and one acid. The essential features of buffer action will be seen from the following example:

An equimolar solution of acetic acid and sodium acetate has a *p*H of about 5. If we add some hydrochloric acid, part of the sodium acetate is converted into sodium chloride, liberating acetic acid. The latter dissociates very little, and the number of free hydrogen ions in the mixture—i.e., the acidity—is not much increased, despite the addition of the hydrochloric acid. If, on the other hand, sodium hydroxide is added instead of HCl it converts some of the acetic acid into acetate, but the remaining acetic acid breaks up into ions until nearly all the hydrogen ions consumed by formation of acetate have been replaced.

In searching for a physiologically harmless buffer with a *p*H of about 2–3, one of us (F. K.) devised a mixture of sodium biphosphate (86 parts) and sodium bisulphate (14 parts), and this is now sold under the name of Optacid. The buffering capacity of the mixture is far greater against acids than against alkalis; but it is right that this should be so because the contents of the stomach have to pass into the duodenum and be made alkaline for tryptic digestion.

Hitherto almost every chemical treatment of hyperacidity is based on the neutralising action of alkaline—or at most neutral—compounds. But complete neutralisation of the contents of the stomach is by no means always desirable, since its effect is inhibition of peptic digestion and often an increased secretion of acid by way of compensation. This defect of alkali therapy has often been pointed out. The commonly used bicarbonate of soda, magnesia usta and magnesium carbonate, are extreme representatives of their class, the *p*H of concentrated solutions varying between 7 and 11. (The insolubility of the magnesium compounds does not prevent suspensions of them from becoming alkaline, as a test with phenolphthalein indicator will show.) In recognition of this objection the alkalinity of remedies recommended has been gradually reduced. Compounds of alumina and silica with alkali came into use; but though they may do something to protect the wall of the stomach their alkalising effect is much reduced—so much so that the usual doses hardly suffice to weaken superacid gastric juice. Greenwald[2] describes a mixture of calcium and magnesium phosphate which was the first remedy to weaken, but not essentially neutralise, the gastric acid. Even this mixture, however, is in itself neutral, and though it counters acidity it does

[1] Körösy, F. (1934) *Tech. Kurir*, **5**; Gerébi, S., and Körösy (1934) *Gyógyászat*, **74**, 146.
[2] Greenwald, I. (1923) *Proc. Soc. exp. Biol., N.Y.* **20**, 436.

nothing to relieve subacidity. Optacid is the first remedy to do both.

The accompanying figure shows the effect of various quantities of (1) sodium bicarbonate, (2) an alum preparation, and (3) optacid on the *p*H of extremely acid gastric juice (from an ulcer patient) in vitro, and illustrates the stability of its action.

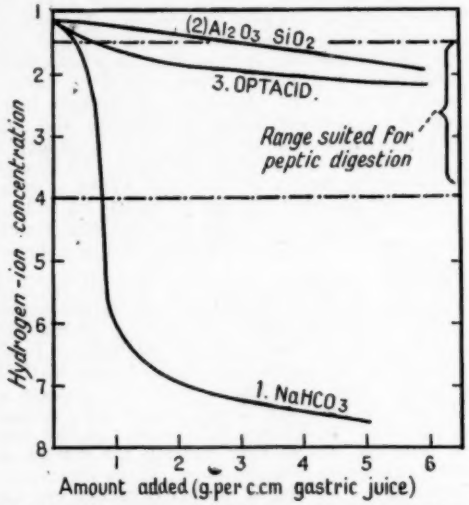


Chart showing changes in the hydrogen-ion concentration of strongly acid gastric juice on addition of various quantities of (1) sodium bicarbonate, (2) an alum-silicate mixture, and (3) optacid.

A similar advantage is gained when the juice is obtained from a stomach secreting little acid: the high initial *p*H is quickly lowered to about 3, but no overdose will reduce it further than 1·6. Test-meals have confirmed the presumption that the ambivalent normalising action of optacid would be the same in the stomach as it is in vitro. Phosphoric acid does not inhibit peptic digestion[3]; the normal dose of optacid was found not to diminish the activity of trypsin in the duodenum.[4] It has also been shown[3,4] that the alkali reserve of the blood is only slightly diminished by very large doses (4 grammes) of optacid, and acidosis therefore need not be feared, though it is wiser not to try the new remedy in patients already acidotic (e.g., in severe diabetes or renal disease). Optacid acidifies the urine, and the acid reaction prevents the possible formation of phosphate stones.

In the treatment of gastric disorders we give optacid in tablets of one gramme or in small granules. One gramme is usually taken at breakfast and two at dinner and supper. Where there is much superacidity we have thought it prudent to give the medicine during or after meals, while for cases with subacidity it is given a few minutes before meals. The tablets are broken into a few pieces and taken in water, and when more than one tablet is used an interval of ten minutes or so is allowed between them. Patients with deficiency of acid usually respond to treatment within a few days, but if pepsin also is absent from the juice it will have to be added. Really serious affections of the mucosa (e.g., in pernicious anæmia) are probably outside the range of the new medicine, and in very severe gastritis the neutral buffer action of mucin can only be overcome by large doses of optacid. The results with superacidity are equally satisfactory, both in ulcer cases and in "functional" disorders. Of 39 patients with peptic ulcer 7 were not benefited however; in 2 of these the secretion of acid was normal, and we think it likely that normal gastric acidity is sometimes sufficient to excite the damaged mucosa of a stomach, so that in these cases of peptic ulcer it may be good treatment to neutralise the gastric acid completely for a time. But for the majority of ulcer patients we prefer our buffer mixture to alkalis. Results obtained mainly in the internal department of the Jewish Hospital, Budapest, among patients under the care of Dr. L. Lévy as chief physician, may be summarised briefly as follows:—

—	Cases examined.	Positive effect.	No effect.
Inacidity and subacidity ..	55	45	10
Superacidity	70	60	10
Ulcus ventriculi and duodeni—			
Superacid	39	34	5
Normacid	2	0	2
Inacid	2	2	0
Heterochylia	7	7	0
Cholecystitis chronica	11	6	5
Colitis chronica	5	0	5
—	191	154 (80%)	37 (20%)

For comparison we append those reported by László,[4] also using optacid, from the II University Medical Clinic in Budapest:—

—	Cases examined.	Positive effect.	No effect.
Inacidity and subacidity ..	40	30	10
Superacidity	34	28	6
Ulcus (superacid)	13	10	3
Chronic cholecystitis	1	0	1
Heterochylia	6	4	2
—	94	72 (77%)	22 (23%)

We conclude that, taking the two hospitals together, this remedy has benefited about 80 per cent. of the patients to whom it has been given, and we hope it will have wider trial.

We are, Sir, yours faithfully,

S. GEREB, M.D.,
F. KŐRÖSY, Ph.D.

Budapest.

[3] Sörensen, S. P. L., and Jürgensen, P. (1909) *Biochem. Z.* **21**, 131; **22**, 352. Róna, P., and Kleinmann, H. (1924) *Ibid*, **150**, 444.

[4] László, G. (1935) *Orv. Hetil.* **79**, 558.

LEEDS GENERAL INFIRMARY.—This hospital, as announced in our last issue (p. 97), has collected the £250,000 which it requires to carry out its plan of improvements and extensions. A pay-block and new blocks for housing the nurses are needed; 140 additional beds are also to be provided for the nursing staff and a sick bay and recreation room.

FALSE CALLS FOR AMBULANCES.—Since Jan. 1st any person who gives false information which would reasonably lead to the dispatch of one of the London County Council's ambulances is liable to a penalty up to £25, unless he can show that he had cause to believe that his information was correct. This provision has been obtained by the London County Council in its General Powers Act of 1936 in view of the large and growing number of false calls, which may have been malicious in origin, received in the last few years by the London Ambulance Service.

PUBLIC HEALTH

VACCINATION IN THE CONTROL OF SMALL-POX

By Duncan Forbes, M.D., D.P.H.
MEDICAL OFFICER OF HEALTH FOR BRIGHTON

There are two types of small-pox: a severe form (variola major) with a mortality of 1 in 5 in unvaccinated persons, and a mild form (variola minor) which is not a killing disease even in the unvaccinated. Both forms breed true. As no Government would dream of enforcing general infant vaccination to control the mild form of the disease, I need only consider the effect of the present Vaccination Acts and regulations upon variola major.

Of first importance is an appreciation of the effect of successful vaccination. If an unvaccinated person, within 48 hours of contact with a case of small-pox, is vaccinated with potent lymph he will not develop small-pox. It is because of this that when a case of small-pox occurs the medical officer of health proceeds to staff his small-pox hospital with nurses, maids, and porters irrespective of whether or not they have been vaccinated. What he never fails to do is to vaccinate the whole staff as soon as possible, and always before 48 hours have elapsed from their first contact with the case of small-pox. It is only because the medical officer can put this cordon of recently vaccinated and therefore immune persons around the small-pox patient that successful isolation is made possible.

Whilst there is then no doubt that a small-pox attack is prevented by recent successful vaccination, the number of years the vaccinated person remains immune is variously stated. The length of this period varies with the individual but depends more or less on the method of vaccination. For instance, a vaccination of four marks resulting in half a square inch of scar, as required of public vaccinators in times gone by, will protect with reasonable certainty for some 10 years and usually longer; whilst a one-mark vaccination with a tiny scar, as allowed by the Vaccination Order of 1929, probably protects for a shorter period. The evidence is more definite regarding the effect of vaccination on the severity of attack after immunity has gone. Tables in the annual report of the medical officer of health of Manchester for 1904 show that the severity of attack varies inversely as the number of vaccination marks and their total scar area. They also demonstrate how little protection is afforded by a one-mark as compared with a four-mark vaccination, the deaths being in the proportion of four mark 1, one mark 5, unvaccinated 9. The figures for scar areas are even more striking—viz., over half a sq. in. 1, under half a sq. in. 10, unvaccinated 19.

Cases of small-pox vary much in their degree of infectivity, but are most infectious in the first few days of the rash. This may be due to the varying extent of the rash on the mucous membranes of the mouth and throat and the incidence of cough leading to rupture of the vesicles and infection by spray. The early infectivity of small-pox is important, as the first cases in a locality may not be diagnosed until the third or fourth day of the rash or later when the vaccination of contacts may fail to prevent secondary cases.

PRESENT METHOD OF CONTROL

When a case of small-pox (variola major) occurs a medical practitioner is almost invariably called in and he either notifies the case as small-pox or calls the attention of the medical officer of health to his suspicion. If the case turns out to be small-pox, within an hour or two of diagnosis, in urban areas where lymph is easily procurable, the home contacts have been vaccinated. Contacts further afield are offered vaccination as soon as possible. The offer of vaccination at the time that contacts are first told of the risk of infection is important, as when offered at once there is a higher acceptance rate; further it leads to a greater proportion of contacts being vaccinated within 48 hours of infection and any attack prevented with certainty. The next step is for the medical officer of health to let all general practitioners in the district know that a case (or cases) of small-pox has occurred and to express his willingness and even anxiety to see any doubtful rashes. This ensures that no cases are overlooked if a doctor is called in.

After the diagnosis of the case and its isolation the most important of all measures for the prevention of spread is the ascertainment of every person who has been in contact with the patient between onset and removal. By careful and repeated inquiries from the patient and his relatives a list of contacts is made out and these are visited daily about the time they are likely to develop the disease. In this way their isolation, should they develop the disease, is ensured practically from the onset. If the supervision of contacts can be, and is, efficiently carried out the small-pox outbreak is quickly brought under control. There are in fact only three ways in which it may escape immediate suppression.

(1) When the attack is so mild that a practitioner is not called in. This happens most frequently in the mild type of small-pox and makes such outbreaks much more difficult to control, especially as there is at times intentional concealment to escape removal to hospital and to prevent loss of time at work. Although mild cases of variola major also occur, due usually to the effect of earlier vaccination and at times to natural resistance to attack, in all but exceptional cases a doctor is called in.

(2) When a practitioner is called in but fails to diagnose the disease and does not think it suspicious enough to report to the medical officer of health; this is the more likely to occur nowadays as many young practitioners have never seen a case of the disease. Under such circumstances a crop of cases may occur before the medical officer hears of the first case, but even then once the presence of small-pox is discovered its spread is quickly controlled.

(3) If the primary case is a tramp or person with no fixed abode, associating with like persons, the contacts cannot be efficiently supervised. Even if a tramp is known to have been in contact with a case of small-pox he cannot be compelled to accept vaccination, to have his movements controlled, or to state his place of destination. Thus the disease may spread via common lodging-houses and casual wards to the general public and be difficult to control.

HISTORY OF INFANT VACCINATION

Although vaccination was made compulsory in 1853 it was not until after the passing of the Acts of 1867 and 1871 that a high percentage of infant vaccination was obtained. Thereafter, for a time, as many as 95 per cent. of infants were vaccinated, but even so it took many years before any large percentage of the population had been vaccinated. In those times when epidemics were frequent compulsory

vaccination was fully justified and was followed by a fall in the incidence of the disease amongst children and adolescents, and later by a fall in case-mortality. Considering the less efficient training and small number of health staffs at that time the continued occurrence of epidemics is not a matter for surprise. If however it had then been realised that vaccination protects from attack for a limited period only and if revaccination at school-leaving age and again in later life had also been made compulsory small-pox could have been controlled by vaccination alone. The compulsory system might indeed have been extended had it not been for the success attending the discovery, immediate vaccination and supervision of all contacts. The work of medical officers of health showed that by these means they could easily have stopped outbreaks in their areas if they had been given power to control the movements of tramps and other migratory persons who were known to have been in contact with small-pox.

Under the circumstances related, a business man would have openly dropped *compulsory* vaccination altogether, he would have given the medical officer of health power to control the movements of migratory contacts, and would have relied upon intensive action by the health staff to prevent spread of the disease. Instead of this, compulsory vaccination was really dropped in 1907, but it was stilled called compulsory and the old cumbersome and expensive methods were retained. Thus whilst the provisions of the Act of 1898 required that objectors had to *satisfy* two justices or a stipendiary magistrate that he conscientiously believed that vaccination would be prejudicial to his child's health, the Act of 1907 only required the parent to make a *statutory declaration* of conscientious objection before a magistrate. Since 1907 vaccinations as a percentage of births have fallen from 71 to 36 and are still falling. Not only so, but in 1929 the central authority, taking unnecessary fright at the possibility of post-vaccinal encephalitis occurring in infants under 6 months of age, recommended a one-mark vaccination by the public vaccinator in place of a four-mark vaccination. In these ways the Vaccination Acts have been rendered useless, first by the reduction of the percentage vaccinated, but mainly by the introduction of inefficient vaccination.

FUTILITY OF THE PRESENT SYSTEM

For years the futility of the present procedure has been recognised, and in 1932 the Law Committee of the Association of Municipal Corporations considered a letter from the Ministry of Health asking them for any proposals they desired to make, in the light of two years' experience of the new regulations, for facilitating the general acceptance of vaccination and preventing the spread of small-pox. They conferred with the Society of Medical Officers of Health and agreed with the recommendation of the latter body that *compulsory* vaccination should be abolished but that facilities should still be provided for vaccination and revaccination against small-pox on a voluntary basis.

In 1934 the British Medical Association set up a committee to consider how best to inform the public of the protection afforded by various methods of immunisation, including vaccination. Their report supported general vaccination and revaccination as important in the prevention of epidemics of small-pox, but added [1]:

"It seems likely that the retention on the Statute Book [of the Vaccination Acts at present in force] will soon serve no practicable purpose. In so far as they foster antagonism to vaccination they hinder the acceptance of other forms of immunisation."

Although all these expressions of opinion must be well known to the Ministry of Health it must be difficult for them to take action unless such action is demanded by public opinion. To help to create this it would be well that the public and particularly parents and magistrates should be informed of the following facts:

The public health service is well able to control outbreaks of virulent small-pox apart altogether from routine vaccination of infants, provided that full powers are given to them to supervise migratory small-pox contacts.

The chance of anyone being infected with virulent small-pox in this country is very remote (1 in 50,000 in my area in the last 25 years). At the same time the parents should bear in mind that if the unvaccinated are infected by virulent small-pox 1 in 5 dies, that the face is greatly disfigured by pock marks, and that efficient vaccination is in the nature of an insurance against such a risk.

As the present one-mark vaccination is of relatively small value parents must ask for two to four marks with a resulting half sq. in. scar area.

The cost of the present system should be estimated and compared with that of a voluntary system from which all unnecessary records are dropped and vaccination carried out at a municipal centre where similar work for immunisation against diphtheria is undertaken. The wastefulness of the present system compared with its small value in both time and money could thus be made apparent and with public opinion in favour of new legislation I have little doubt that at no distant date the present Acts would be repealed, a purely voluntary system introduced, and greater powers given to medical officers of health to keep migratory contacts under supervision.

[1] *Brit. med. J.* 1935, I, 292 (Supp.).

INFLUENZA

THE number of deaths from influenza reported from the Great Towns in the week ending Jan. 9th, 1937, was 768—a figure for which the recent trend of the outbreak had prepared us.

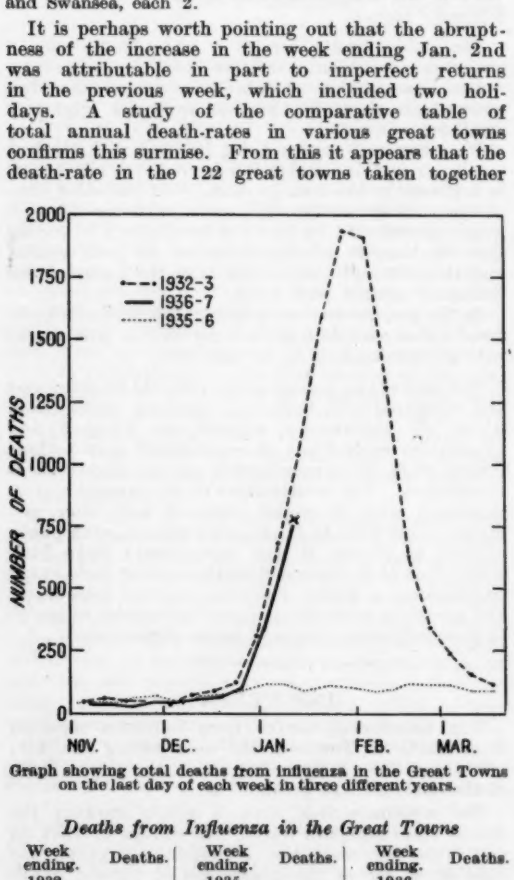
We reproduce this week a graph showing the deaths from influenza during the winters of 1932–33 and 1935–36, with the corresponding graph for 1936–37 so far as the figures are at present available. (The data from which the graph is drawn are given at the foot.) As the weeks do not strictly correspond in the three years we have plotted the deaths against the last day of the week to which they relate in each year. It should be borne in mind that the graph relates only to deaths and not to attacks, and there is evidence from all parts of the country that the disease is still taking a mild form, with the normal age-distribution, and no emphasis on young adults as in the pandemic of 1918. The line for 1937 runs so far closely parallel to that for 1933.

Of the 768 deaths from influenza reported in the week ended Jan. 9th, 1937, 558 were in the south-eastern area (including London), 98 in the Midlands, 87 in the north, 18 in Wales, 5 in the south-west, and 2 in the eastern counties.

Of the 325 deaths from influenza reported in the week ended Jan. 2nd, 1937, 128 occurred in London and 232 in Greater London. The numbers in the Outer Ring were in diminishing order: Willesden, 12; Ealing, 9;

Hendon, 7; West Ham, 6; Walthamstow, 5; Acton and Hornsey, each 4; Brentford, 3; East Ham, Harrow, Leyton, Southgate, and Wembley, each 2; Barking, Beckenham, Enfield, Mitcham, Wimbledon, and Wood Green, each 1. Outside London the number of deaths in diminishing order was as follows: Bristol, 17; Bradford, 10; Leeds, 9; Birmingham, 8; Northampton, 7; Nottingham, 6; Leicester, 5; Manchester, Cardiff, and Rhondda, each 4; Reading, Southend-on-Sea, and Liverpool, each 3; Brighton, Canterbury, Hove, Sunderland, Derby, Ipswich, and Swansea, each 2.

It is perhaps worth pointing out that the abruptness of the increase in the week ending Jan. 2nd was attributable in part to imperfect returns in the previous week, which included two holidays. A study of the comparative table of total annual death-rates in various great towns confirms this surmise. From this it appears that the death-rate in the 122 great towns taken together



Graph showing total deaths from influenza in the Great Towns on the last day of each week in three different years.

Deaths from Influenza in the Great Towns

Week ending.	Deaths.	Week ending.	Deaths.	Week ending.	Deaths.
1932		1935		1936	
Dec. 3rd	33	Nov. 30th	58	Nov. 28th	44
„ 10th	68	Dec. 7th	45	Dec. 5th	43
„ 17th	85	„ 14th	62	„ 12th	54
„ 24th	120	„ 21st	67	„ 19th	57
„ 31st	303	„ 28th	80	„ 26th	97
1933		1936		1937	
Jan. 7th	680	Jan. 4th	110	Jan. 2nd	325
„ 14th	1039	„ 11th	110	„ 9th	768
„ 21st	1588	„ 18th	89	„ 16th	
„ 28th	1933	„ 25th	104	„ 23rd	
Feb. 4th	1909	Feb. 1st	98	„ 30th	
„ 11th	1306	„ 8th	85	Feb. 6th	
„ 18th	630	„ 15th	97	„ 13th	
„ 25th	344	„ 22nd	119	„ 20th	
Mar. 4th	242	„ 29th	107	„ 27th	
„ 11th	157	Mar. 7th	112	Mar. 6th	
„ 18th	119	„ 14th	84	„ 13th	
„ 25th	65	„ 21st	86	„ 20th	

increased from 10·8 to 17·0, but as the figures for the two previous December weeks were 12·4 (Dec. 12th) and 13·3 (Dec. 19th) it seems not unlikely that the actual rise in the death-rate between Dec. 26th and Jan. 2nd is nearer 2 than 5. Applying the same adjustment to the other figures in the same table, it is clear that while there has been a sharp rise in London and Bristol, and a less but still material rise in Bradford, Liverpool, and Nottingham, the increase in the death-rate at such places as Birmingham, Manchester, and Newcastle-on-Tyne may be more apparent than real.

THE SITUATION IN LONDON

The number of beds allocated to influenza in the L.C.C. fever hospitals is now 700. On Saturday, Jan. 9th, there were over 1600 cases in the general hospitals and 513 in the fevers. This is an increase over the previous week, but from the returns of admissions it does not appear that the demand for hospitalisation is increasing. The number of patients remaining under treatment will of course continue to increase until the discharges are greater than the admissions. The Registrar-General's figures for the week ending Jan. 9th show 311 deaths certified as due to influenza in London compared to 128 in the preceding week. Notifications of acute primary or influenzal pneumonia were 408 in the week ending the 9th, compared with 290 in the previous week. The clinical picture remains much the same; there is no evidence that pneumonia is occurring with more than average frequency or manifesting the dreaded toxic attributes of the 1918 pandemic. A considerable degree of prostration and depression seems to persist for some days after the temperature has fallen to normal. Many of the L.C.C. nursing staff are still incapacitated.

NEWS FROM THE COUNTRY

The information given last week has been substantially confirmed since, except that Nottingham and its neighbour Loughborough seem now to have suffered as severely as any places outside London. In Birmingham the disease though widespread has remained mild. Bradford is reported to have suffered most among the Yorkshire towns, transport drivers and other officials having been down in large numbers, but as elsewhere attacks were of minor severity and short duration. In Leeds also the public utility services have been much inconvenienced. Around Newcastle-on-Tyne there has been a slight increase in febrile illnesses but nothing which can be called an epidemic, while the outbreak of nausea and vomiting has definitely subsided; deaths from pneumonia are not above the average for the time of year. At Brighton the epidemic is still active but not increasing; as time goes on there are more relapses, the depression however if severe does not last long. Here as elsewhere the few cases of sequential pneumonia have not been severe or toxic.

ACUTE POLIOMYELITIS

THE Ministry of Health has issued a revised memorandum (166/Med. 2*d*.), the text of which follows closely that of the original, published in 1932, but differs in important particulars which reflect the growth of our knowledge of poliomyelitis during the past four years. Since the first memorandum was published America and Australia have added most to our knowledge of the epidemiology of poliomyelitis and England the least, for the satisfying reason that the disease is less frequent in Britain than in any other part of the civilised world. The memorandum states: "There is no sufficient reason to believe that the virus of poliomyelitis is conveyed to man by foodstuffs or insects, or that the disease is associated with insanitary conditions." These words are identical in both issues, but whereas in 1932 there was no

proof that the virus is conveyed in these ways, in 1936 there is strong evidence that it is not. Differences in the paragraphs on epidemiology and pathology are due to the Ministry accepting the conclusion of the neurologists that poliomyelitis is primarily an infection of the neurons directly through the filaments of the olfactory nerves. Formerly it was believed that the course of the disease was: nasal catarrh, septicæmia, invasion of meninges, and lastly implication of the neurons—and that the disease could stop at any of these stages. In other words, that poliomyelitis is an acute fever which may or may not have infantile paralysis as a complication. The new view is that poliomyelitis is a direct infection of the neurons, which may or may not lead to permanent paralysis, but there is no disease without implication of the neurons. It is well to keep open the question whether man may react otherwise than by poliomyelitis to the virus, but it may be accepted that unless the neurons are implicated at the start, they never will be. The memorandum mentions that the cephalic form (polio-encephalitis) usually ends in death or complete recovery, though it does not always do so. The paragraph on treatment in the new memorandum differs from that in the old more in tone than in words, owing to the fact that in 1932 convalescent serum gave great promise, whereas, unfortunately, in 1936 hope of serum treatment had fallen almost to zero. "The after-effects of poliomyelitis are of so grave a nature that in spite of these findings some medical practitioners may still desire to use serum." This is not encouraging, but it may be the best that can be said with truth. There is no material alteration in the paragraphs on precautions against infection and on the action by the medical officer of health. It is doubtful whether any of the precautions is of much avail. Since in epidemic centres passive carriers are vastly more numerous than cases or known contacts, isolation does not promise much; but the evidence from Queensland that contacts are mainly responsible for the spread of the disease is not to be ignored. It has been questioned whether actual sufferers can spread the disease after symptoms have developed. The late James Collier held that they could not. We are told "Neither serum nor specific vaccines can be recommended for individual protection." While we do not cavil at this statement in 1936, we may well hope that the future will give us a vaccine which is both trustworthy and free from danger.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED JAN. 2ND, 1937

Notifications.—The following cases of infectious disease were notified during the week: Small-pox, 0; scarlet fever, 1933; diphtheria, 1353; enteric fever, 18; pneumonia (primary or influenzal), 1542; puerperal fever, 46; puerperal pyrexia, 150; cerebro-spinal fever, 33; acute poliomyelitis, 2; encephalitis lethargica, 3; continued fever, 1 (Brighton); dysentery, 16; ophthalmia neonatorum, 74. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on Jan. 8th, 1937, was 3805, which included: Scarlet fever, 953; diphtheria, 1041; measles, 15; whooping-cough, 498; puerperal fever, 14 mothers (plus 5 babies); encephalitis lethargica, 285; poliomyelitis, 4. At St. Margaret's Hospital there were 13 babies (plus 6 mothers) with ophthalmia neonatorum.

Deaths.—In 122 great towns, including London, there was no death from small-pox, 1 (1) from enteric fever, 7 (0) from measles, 6 (0) from scarlet fever, 28 (7) from whooping-cough, 44 (5) from diphtheria, 52 (17) from diarrhœa and enteritis under two years, and 325 (128) from influenza. The figures in parentheses are those for London itself.

Nottingham had 3 deaths from whooping-cough. Fatal cases of diphtheria were reported from 25 great towns, Liverpool and Birmingham each 4.

The number of stillbirths notified during the week was 302 (corresponding to a rate of 44 per 1000 total births), including 44 in London.

THE SERVICES

ROYAL NAVAL MEDICAL SERVICE

Surg. Comdr. G. Kirker to *Pembroke* for R.N.B.

Surg. Lt.-Comdr. C. Ommanney-Davis retires at own request.

Surg. Lt. (D) F. J. Goldsworthy promoted to rank of Surg. Lt.-Comdr. (D).

C. E. Fitton, H. W. Gibbs, and R. A. Hilton to be Surg. Lts. (D).

Surg. Lt. C. J. Mullen to *Drake* for R.N.B.

Surg. Lt. D. Ewart transferred to Emergency List.

The following have received appointment as Surg. Lts. for Short Service: W. Boyd (Glasgow Univ.), F. A. Crosfill (Leeds Univ.), G. C. Denny (Guy's Hosp.), F. P. Ellis (Manchester Univ. and Charing Cross Hosp.), R. Vaughan Jones (Birmingham Univ.), W. Sloan Miller (Glasgow Univ.), L. R. Norsworthy (St. Bartholomew's Hosp.), B. O'Neill (Cork Univ. Coll.), G. R. Rhodes (Manchester Univ.), and P. G. Stainton (Guy's Hosp.); and appointed to R.N. Hosp., Haslar, for course.

G. H. C. R. Critien entered as Surg. Lt. for short service.

ROYAL NAVAL VOLUNTEER RESERVE

Surg. Lts. W. S. Miller and R. V. Jones, commissions terminated on transfer to R.N.

ROYAL ARMY MEDICAL CORPS

Maj.-Gen. H. Ensor, C.B., C.M.G., C.B.E., D.S.O., ret. pay (late R.A.M.C.), is apptd. Col. Comdt., vice Maj.-Gen. O. L. Robinson, C.B., C.M.G., ret. pay (late R.A.M.C.), who has attained the age limit for his appt.

Capt. T. F. M. Woods to be Maj.

TERRITORIAL ARMY

Supernumerary for service with the O.T.C.: Lt.-Col. J. du P. Langrishe, D.S.O. (Lt.-Col. Res. of Off.), resigns his commn. in the T.A.

ROYAL AIR FORCE

Wing Comdr. R. H. Stanbridge to Princess Mary's R.A.F. Hospital, Halton, for duty as medical officer.

Flight Lts. P. A. Cooper to No. 31 (Army Coöperation) Squadron, Karachi, India; C. M. Fraser and J. F. McGovern to Central Medical Establishment, London; and W. P. Stamm to R.A.F. Station, Abbotsinch.

Dental Branch.—Flight Lt. J. E. Tyrrell to R.A.F. Station, Calafrana, Malta.

Flight Lt. P. J. Clifford Keane is transferred to the Reserve class D.

INDIAN MEDICAL SERVICE

Majs. to be Lt.-Cols.: L. G. Pearson and P. M. Antia.

The undermentioned appts. are made:—

To be Capt. (on prob.): A. H. O'Malley.

To be Lts. (on prob.): A. M. McGavin, J. D. O'Shaughnessy, J. E. O'Donnell, and D. R. Cattanach.

The undermentioned appt. has been made in India:—

D.A.D.M.S.: Bt. Lt.-Col. A. H. Craig, I.M.S.

The undermentioned officers have vacated appts. in India:—

D.A.D.P.: Lt.-Col. A. C. Craighead, I.M.S.

D.A.D.M.S.: Lt.-Col. C. A. Wood, M.C., I.M.S.

FOR AMATEUR ACTORS AND PRODUCERS.—A practical course of acting, play-production, and stage craft will be held at the Everyman Theatre, Hampstead, on Sunday afternoons, Feb. 7th, 21st, 28th, and March 14th, 21st, and 28th. During April and May a series of public performances will be given by members of the course. Further particulars may be found in our advertisement columns.

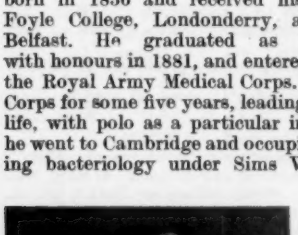
OBITUARY

SIR DAVID SEMPLE, M.D. R.U.I.

LATE DIRECTOR OF THE PASTEUR INSTITUTE, INDIA

THE death occurred on Thursday, Jan. 7th, in St. Mary's Hospital of Sir David Semple, who will always be remembered in association with antirabies therapeutics, and whose general contributions to tropical medicine were of the first order.

David Semple was the second son of the late William Semple of Castlederg, Co. Tyrone. He was born in 1856 and received his early education at Foyle College, Londonderry, and Queen's College, Belfast. He graduated as M.D., M.Ch. R.U.I. with honours in 1881, and entered almost immediately the Royal Army Medical Corps. He served with the Corps for some five years, leading an active regimental life, with polo as a particular interest. But in 1893 he went to Cambridge and occupied his leave by studying bacteriology under Sims Woodhead. He then began his association with Sir Almroth Wright, under whom his later bacteriological work was done, and when Sir David Bruce left for S. Africa to carry out his brilliant studies of the tsetse fly, Semple was selected by Wright as Bruce's successor to be assistant professor at Netley. He proved a good teacher, while he collaborated closely with Wright in the early work on typhoidinoculation and on Malta fever, during which latter investigation both the researchers contrived to infect themselves. At Netley Semple gained his early insight into Pasteur's antirabic work, for at this time Pasteur's methods were a regular subject of demonstration to the students at the Army Medical School. When his appointment at Netley was up he went to Paris and studied the antirabic treatment at the Pasteur centre, so that on proceeding to India in 1899 he was especially well equipped for the important opening which now came to him.



SIR DAVID SEMPLE

[Photograph by Elliott & Fry

We owe to Sir Rickard Christophers the following full summary of Sir David Semple's work in India.

"Though it is now more than twenty years since Sir David Semple retired from active work in India his name will be fresh in the minds of a great many who knew him personally and an even greater number who knew him by reputation. Few in the medical services in India have ever been so well and widely known, personally and by reputation. He was the father of antirabic treatment in India and came to be regarded almost as a seer by many thousands of Indians and hundreds of Europeans who in the course of years have travelled to Kasauli to receive antirabic treatment or advice. But this is not the only reason why Sir David Semple's name was well known. Coming to India at a time when there was practically no organisation for medical research in that country and no such thing as courses of instruction as at present in schools of tropical medicine at home Sir David Semple as teacher and organiser for many years represented all that was most modern and progressive in scientific medicine and an inspiration not only to those of his own service in India but even more so perhaps to many young Indian Medical Service officers with whose work his own became increasingly associated. He was definitely the founder of the two institutes at Kasauli, the Pasteur Institute of India and the Central Research Institute, and as such played a very considerable part in the eventual development of medical research in India, since from both these institutes have come many of the future directors of the now numerous laboratories, and Pasteur institutes that have since arisen in various parts of India.

"There can be little doubt that Sir David Semple's success in India was in considerable part at least due to the time he had spent before arriving in that country as assistant professor of pathology at Netley with Sir Almroth Wright, and to his work under Pasteur at Paris. Trained in such an environment he came equipped not only with a sound knowledge of bacteriology and bacteriological and serological technique but also imbued with the spirit of a new revival in medical research which had begun to be evident at this time. Very probably, the present writer thinks, Semple must have been sent to Paris with the definite object of enabling him to put into concrete form a scheme for a Pasteur institute in India which had already been some time under consideration, and in which Sir Almroth's advice had at some previous time been asked. Whether this be so or not, David Semple in 1899 came out to India equipped as few before him had been to take charge of activities in a virgin field. On April 9th, 1900, the Pasteur Institute of India was opened with Sir David Semple (then Major Semple) as director. In the first year some three hundred patients were treated. It is impossible to read the early annual reports of this new institute, the first of its kind in the British Empire, without being deeply impressed not only with the energy and initiative displayed by its founder, but also by the enlightened spirit which evidently actuated him in all the work done. Looking back one sees even in the early years of the Institute's existence the original birth of activities which have since grown but which are still much as started by Semple. The production and issue of antivenine—a serum prepared against cobra bite, and later including also protective properties against the dreaded Daboia or Russell's viper—had already been started even as early as 1903. A serum against rabies (as distinct from a protective vaccine), now used in certain cases, had already been prepared and tried. Antityphoid vaccine and even diphtheria and tetanus serum were likewise prepared and the use of the laboratory for diagnostic purposes to assist R.A.M.C. and I.M.S. officers and private practitioners was already in 1903 recognised. An entirely new type of institute, such as is now familiar enough, had thus been created for the first time in India and probably for the first time in any tropical British Possession.

"Schemes for more effective laboratories in India had however for some time been receiving increased attention and under the régime of Lieut.-Colonel Leslie, Sanitary Commissioner with the Government

of India, there was brought about the formation of a bacteriological department with recognised laboratories for the Central and Provincial Governments and a fixed bacteriological cadre much as has since existed. In this scheme Semple became the first director of the Central Government's laboratory, the Central Research Institute, at Kasauli. It was again due to Semple's personal energy and capacity for organisation that this institute came into being and continued to function not only as a centre for research but one from which a spirit has been infused that has had a great directive influence on the future development of medical research in India.

"During his time as director of this new institute Sir David Semple made some important contributions to medical science. Among such may be mentioned the results of an inquiry into the methods by which enteric fever was contracted in the British Army in India, results which greatly modified the existing outlook on the causes of this disease among troops and the steps to be taken to prevent it. Perhaps the research of greatest practical importance was that which dealt with the protective properties of carbolised dead vaccine in rabies. He showed that such vaccine could be used with effect in place of the living virus which was the basis both for the 'dried cord method' and the 'dilution method' then in use. Adoption of this form of the antirabic treatment has completely modified previous ideas as to the necessity of the patient travelling long distances to be treated in a hill station, and has allowed of the present method of distribution of the vaccine to numerous inoculation centres in the plains.

"It is not, however, as the pure research worker that Semple was chiefly known, but rather in the rôle of inspired organiser and teacher. As the former he built well and laid an enduring basis on which others have since extended the work. As a teacher his power lay in a great faculty amounting to genius for simple demonstration. He had the one prime necessity for the good teacher that he never forgot that those being taught did not start with all the knowledge he himself possessed. To those who knew him in private life and to those about him in the laboratory he was a staunch and kindly friend and his memory will long remain in Kasauli where he spent so many years of his life."

Sir David Semple was knighted in 1911 and retired from service in India in 1913, being appointed director-general of the Public Health Department in Egypt. He served in Egypt throughout the war with the rank of Colonel A.M.S. and received the Order of the Nile. He married Ethel May, daughter of Dr. Edward Watson of Isleham, Cambs, and was the father of seven children of whom three daughters survive. Of four sons two were killed in the war and two died in youth.

THE LATE SIR GRAFTON ELLIOT SMITH

Dr. A. J. E. Cave, assistant conservator of the museum of the Royal College of Surgeons of England, writes: "The outstanding achievements of the late Sir Grafton Elliot Smith in the field of cultural anthropology may be less familiar to his medical brethren than are his pioneer investigations into mammalian cerebral anatomy, or his important contributions to the physical anthropology of primitive and of fossil man. Yet his influence in this particular field (one of increasing social and politico-economic importance) has been as profound as that of a Darwin or a Huxley in realms biological: indeed, no more may the modern ethnologist neglect a thoughtful recognition of Elliot Smith's doctrine of the diffusion of culture than the present-day biologist may dispense with some scheme at least of organic evolution.

"The potent influence which Elliot Smith was later to exert had its seeds in his chance occupancy of the Cairo chair of anatomy, which brought him into close and sympathetic coöperation with the foremost Egyptian archæologists of his day (Maspero, Junker, Reissner, Mace, Quibell, Theodore M. Davis, and others) and gave him an unrivalled acquaintance with Egyptian cultural elements of all periods of that country's history. His anatomical skill was sought increasingly in the description and recording of extensive series of human remains (cf. his contributions to the *Bulletins* of the Archæological Survey of Nubia), and in the examination of many historic and other mummies, the volume on 'The Royal Mummies,' of the Cairo Museum Catalogue, being from his pen. His numerous memoirs on mummification (continued in after years) not only gave us the first truly scientific and comprehensive analysis of this curiously distinctive practice, but also focused their author's attention sharply upon a ritual which he recognised as constituting the central nucleus of the whole of ancient Egyptian civilisation. Elliot Smith intuitively perceived in the practice of mummification one of the master themes of cultural anthropology, a theme which he expanded and elaborated in later years to most fruitful purpose. It was, originally, from the mere geographical distribution, past and present, of this peculiar and difficult practice that he demonstrated (1915) 'The Migrations of Early Culture,' a classic of ethnological accomplishment.

"He sought increasingly, with his colleague, Dr. W. J. Perry, and the disciples they gathered about them, corroborative evidence of the actual spread of cultural elements and customs from one original home, and whilst such evidence accumulated, he proclaimed, with characteristic fullness and vigour, his provocative ethnological doctrine of the 'diffusion of culture.' Tremendous, even bitter, was the opposition to this novel teaching, and the echoes of conflict are still about our ears. But in the main, the old fallacy of a basic 'psychic unity' underlying human activities and reactions was exploded, and the gist of later anthropological investigation has been a confirmation of the truth and reality of the main tenets at least of the diffusionist gospel and of Elliot Smith's penetrating conception regarding the fundamental uniformity of early civilisations. The whole face of ethnological study has been renewed, and a new and vivifying spirit infused therein.

"It is to Elliot Smith's lasting credit that he, first, with an intuition transcending the merely anatomical, perceived in Ancient Egypt the essential threads of primitive culture and civilisation and out of them wove, on the loom of his genius, the tapestry of human history."

CONGRESS OF FEVER THERAPY.—As announced in our issue of Dec. 26th, the first International Congress of Pyretotherapy will be held at Columbia University, New York, on March 29th, 30th, and 31st. We are informed that Dr. Germain Blechmann, 30, avenue de Messine, Paris VIII, is drawing up a report on pyretotherapy in pædiatrics and asks that all interested should send him their publications on this subject and a résumé of communications they would like to put before the congress. The English secretary for the congress is Dr. W. Kerr Russell, 126, Harley-street, London, W.1, and the secretary-general Dr. William Bierman, 471, Park-avenue, New York.

MEDICAL NEWS

University of London

On Tuesday, Jan. 19th, Prof. J. C. Drummond will give the first of six weekly lectures on problems of nutrition, and on Monday, Jan. 25th, Mr. H. R. Ing, D.Phil., will give the first of six lectures on chemical structure and pharmacological action. These lectures will all be held at 5 P.M. at University College, Gower-street, W.C. Five Heath Clark lectures on the development of bacteriology with some account of the pioneers who have made it a science will be given at the London School of Hygiene, Keppel-street, W.C., on Jan. 25th, 28th, and Feb. 1st, 4th, and 8th, at 8 P.M., by Dr. William Bulloch, F.R.S., emeritus professor of bacteriology in the University. On Tuesdays, Feb. 9th, 16th, and 23rd, at St. Mary's Hospital medical school, at 5.30 P.M., Mr. E. D. Telford, emeritus professor of systematic surgery in the University of Manchester, will lecture on some disorders of the peripheral circulation. They are open to all interested in the subjects.

The following have been recognised as university teachers at the schools indicated: Mr. J. P. Hosford, Dr. James Maxwell, and Dr. A. W. Spence (St. Bart.'s); Dr. J. D. Benjafield, Mr. Ralph Marnham, and Mr. T. F. McNair Scott (St. George's); Mrs. Joan Taylor (Royal Free); Mr. B. W. Fickling and Mr. D. G. Walker (London School of Dental Surgery); Mr. Percival Hartley, D.Sc., and Sir Patrick Laidlaw (National Institute for Medical Research).

At recent examinations the following candidates were successful:—

M.D.

Branch I (Medicine).—J. A. Brocklebank, Guy's Hosp.; A. M. R. Cann, Middlesex Hosp.; E. A. Danino, St. Bart.'s Hosp.; C. J. Gavey, London Hosp.; N. M. Green, Univ. Coll. Hosp.; R. R. Henderson, A. L. P. Jeffery, and Evan Jones, St. Thomas's Hosp.; E. I. Jones, King's Coll. Hosp.; F. A. Jones, St. Bart.'s Hosp.; A. L. Light, Univ. of Leeds; G. A. M. Lintott, Guy's Hosp.; Mary F. Lockett, Roy. Free Hosp.; Brian McArdle, Guy's Hosp.; D. C. Reavell, St. Bart.'s Hosp.; A. M. Stewart-Wallace, Univ. Coll. Hosp.; and J. B. L. Tombleson, St. Thomas's Hosp.

Branch II (Pathology).—G. J. Cunningham and A. H. T. Robb-Smith (university medal), St. Bart.'s Hosp.

Branch III (Psychological Medicine).—A. C. Dalzell (university medal), King's Coll. Hosp.

Branch IV (Midwifery and Diseases of Women).—Agnes V. Kelynack, Roy. Free Hosp.; L. W. Lauste, St. Thomas's Hosp.; G. G. Macdonald, Univ. Coll. Hosp.; Marjorie E. Roberts, Roy. Free Hosp.; J. W. Schabort, Guy's Hosp. and Postgraduate Medical School; and Violet H. Whapham, Roy. Free Hosp.

Branch V (Hygiene).—Karl Biden-Steele, Guy's Hosp.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty held on Jan. 4th, with Prof. Archibald Young, the president, in the chair, the following were admitted to the fellowship:—

Jacques Simon Cramer (Fiji); Rustom Ardeshir Davar (London); Alexander Hutchison and Agnes Thomson Kennie (Glasgow); Sydney Mander Laird (Kilmacolm); Patrick Joseph Molloy (Glasgow); Benoy Bhusan Mukerjee and Charu Chandra Saha (London); and Tanjore Somosundara Subramaniam (Liverpool).

International Surgical Congress

The next congress of the International Surgical Society is to be held in Vienna in 1938, and arrangements are now being made. The subjects of discussion will be the surgical treatment of arterial hypertension, bone-grafts, and the surgical treatment of cysts and pulmonary tumours. Members of the society who would like to take part are asked to communicate with Prof. Grey Turner at the British Postgraduate Medical School, Ducane-road, London, W.12.

Conference on the Accredited Milk Scheme

On Jan. 28th, as already announced, the Royal Sanitary Institute is holding a discussion on the administration of the Milk (Special Designations) Order, 1936, with respect to accredited milk. A large attendance is expected, and it has therefore been decided to transfer the meeting from the house of the institute to the Central Hall, Westminster. It begins at 2 P.M. Mr. Thomas Baxter, chairman of the Milk Marketing Board, will preside, and Dr. W. G. Savage, medical officer of health for Somerset, will open the discussion.

THE American Congress of Physical Therapy has awarded to Dr. Stefan Jellinek, professor of electropathology in the University of Vienna, its gold key for distinguished service, and has elected him an honorary life member. A note describing Prof. Jellinek's museum of electropathology was published in our issue of Nov. 14th, 1936, p. 1195.

Research in Encephalitis

The foundation of the advancement of encephalitis research, at the University of Berne, offers prizes to workers in that field. Particulars will be found in our advertisement columns.

Hunterian Society

The Hunterian lecture of this society will be delivered at the Mansion House, London, at 9 P.M. on Monday, Jan. 18th, by Dr. J. Schoemaker of The Hague. He will speak on the surgery of gastro-duodenal inflammation.

Royal Microscopical Society

The annual meeting of this society will be held at B.M.A. House, Tavistock-square, London, W.C., on Wednesday, Jan. 20th, at 5.30 P.M., when Mr. R. S. Clay, D.Sc., will deliver a presidential address on the mechanical development of the microscope.

A Hospitals Emblem

Hospitals Week in London and Greater London is timed for May 2nd–8th, immediately before the Coronation. Over 80 hospitals are uniting in a combined attempt to raise funds, and this will take the place of the flag days previously scattered throughout the year. The committee organising Hospitals Week, whose chairman is Lord Luke, is in search of an emblem that can be made as familiar to the public as the red cross and the Flanders poppy. Suggestions may be addressed to the hon. secretary, Hospitals Week, 36, Kingsway, London, W.C.2, but no prizes are offered.

B.M.A. Scholarships and Grants in Aid of Research

The Council of the British Medical Association is prepared to receive applications for research scholarships and grants for assistance of research in connexion with disease.

Scholarships.—An Ernest Hart memorial scholarship, of the value of £200 per annum, a Walter Dixon scholarship, value £200 per annum, and three research scholarships, each of the value of £150 per annum. These scholarships are given to candidates whom the Science Committee of the Association recommends as qualified to undertake research in any subject relating to the causation, prevention, or treatment of disease. Preference will be given, other things being equal, to members of the medical profession. Each scholarship is tenable for one year, commencing on Oct. 1st, 1937. A scholar may be reappointed for not more than two additional terms, and is not necessarily required to devote whole time to the work of research, but may hold a junior appointment at a university, medical school, or hospital, provided the duties of such appointment do not interfere with the work as a scholar.

Grants.—Grants for the assistance of research into the causation, treatment, or prevention of disease will be made. Preference will be given, other things being equal, to members of the medical profession and to applicants who propose as subjects of investigation problems directly related to practical medicine.

Applications for scholarships and grants must be made not later than Saturday, May 8th, 1937, on the prescribed form, a copy of which will be supplied on application to the medical secretary of the Association, B.M.A. House, Tavistock-square, London, W.C.1. Applicants are required to furnish the names of three referees who are competent to speak as to their capacity for the research contemplated.

The Council will also consider the award of the Katherine Bishop Harman prize for the year 1938. The purpose of the prize, the value of which is £75, is the encouragement of study and research in connexion with risks of pregnancy and childbearing, and the competitor, who may be any registered medical practitioner, is left free to select the work to be presented, provided it comes within the indicated terms. The essay must be typewritten or printed in the English language, distinguished by a motto, and accompanied by a sealed envelope bearing the same motto and enclosing the candidate's name and address.

Selly Oak Hospital

Birmingham city council have approved large extensions to this hospital which will cost over £250,000.

A Woman Police Surgeon

It is announced that Dr. Eleanor Margaret Reece has been appointed a divisional police surgeon to the Metropolitan Police Force. This is the first appointment of a woman doctor to a post of this kind by Scotland Yard.

Society for Relief of Widows and Orphans of Medical Men

At a quarterly court of directors held on Jan. 6th, with the president, Mr. V. Warren Low, in the chair, six new members were elected, and one death and one resignation reported. A sum of £1540 was voted from the ordinary funds, and one of £541 from the Brickwell fund, for the payment of the half-yearly grants to the 59 widows and 9 orphans in receipt of relief. It was reported that £640 had been distributed in Christmas presents, each widow receiving £10 and each orphan £5; this in addition to their ordinary grants. Particulars and application forms for membership from the secretary of the society at 11, Chandos-street, London, W.1.

Fellowship of Medicine and Post-Graduate Medical Association

From Jan. 25th to 30th there will be an all-day course in chest diseases at the Brompton Hospital. An intensive course in gynæcology will be given at the Chelsea Hospital for Women (Feb. 8th to 20th), and a course in medicine, surgery, and gynæcology at the Royal Waterloo Hospital (Feb. 22nd to March 6th). A week-end course will be held at the Princess Elizabeth of York Hospital for Children on Feb. 20th and 21st. M.R.C.P. courses will be given as follows: clinical and pathological course at 8 P.M. on Tuesdays and Thursdays at the National Temperance Hospital (Feb. 16th to 25th); chest diseases at 5 P.M. two evenings weekly at the Brompton Hospital (Feb. 22nd to March 20th); heart and lung diseases at 8 P.M. on Mondays, Wednesdays, and Fridays at the Royal Chest Hospital (March 1st to 20th); and afternoon neurology course at the West End Hospital for Nervous Diseases (March 8th to 20th). A course in anatomy and physiology in preparation for the primary F.R.C.S. examination will be given at 5.15 P.M. on Mondays, Wednesdays, and Fridays from Feb. 22nd to May 24th at the Infants Hospital, Vincent-square. Surgical tutorial classes for F.R.C.S. (final) candidates are being given at the National Temperance Hospital at 8.30 P.M. on Tuesdays and Thursdays. Further information may be had from the secretary of the fellowship, 1, Wimpole-street, W.1.

Memorial to Dr. R. J. Gittins

An extension to the pathological department of the Birmingham Children's Hospital was opened on Jan. 6th by the deputy mayor of Birmingham, Mr. Alderman S. J. Grey. The additional storey, which has cost £3500, brings the pathological and biochemical departments under one roof and provides a biochemical laboratory, 34 ft. by 15 ft., a museum and library, 21 ft. by 15 ft., and separate rooms for balances, washing up of bottles, and equipment. There is an office and workroom for the pathologist, and an office and workroom for the head biochemist, with cloak-room accommodation for the department. The ground floor has been reorganised and contains a large pathological laboratory, with two separate workrooms for research scholars, a post-mortem room, refrigerator room for bodies, a mortuary chapel, and a record room. The old biochemical department adjacent will serve for making routine media, sterilisation, &c., a second room for X ray equipment, for animals, sections, and bodies, and a third as a photographic department with dark room for Price-Jones apparatus.

The extension has been erected to the memory of the late pathologist to the hospital and a memorial tablet was unveiled bearing the following inscription:—

"This tablet records the extension of the Pathological Department in memory of Robert John Gittins, M.D., M.R.C.P., D.T.M. & H., who rendered devoted service to the Hospital as Pathologist from 1930–1934, and gave his life in an unavailing attempt to save his son from drowning on 7th October, 1934."

Maternity and Child Welfare Conference

The seventh English-speaking Conference on Maternity and Child Welfare will be held at B.M.A. House, Tavistock-square, London, W.C., on June 1st, 2nd and 3rd under the presidency of Sir Kingsley Wood, Minister of Health. The idea running through the whole conference is to be the further evolution of the maternity and child welfare movement throughout the British Empire and the United States of America. Further information may be had from the secretary of the National Association for the Prevention of Infant Mortality (Carnegie House, 117, Piccadilly, London, W.1) which is arranging the conference on behalf of the National Council for Maternity and Child Welfare.

British Empire Cancer Campaign

Sir Cuthbert Wallace, P.R.C.S., presided at the sixty-first quarterly meeting of the grand council of the British Empire Cancer Campaign held in London last Monday. The council tendered its sympathy to Lady Bland-Sutton in her recent bereavement; the late Sir John Bland-Sutton was one of the founders of the campaign, and was vice-chairman of the grand council for ten years. Mr. Stanford Cade, F.R.C.S., of the Westminster Hospital, was invited to become a member of the grand council, and Sir Harold Mackintosh and Mr. B. T. Clegg were invited to represent the Yorkshire council in addition to Lord Harewood.

The following grants, in addition to those totalling £28,995 which were made at the annual general meeting in November, were approved on the recommendation of the scientific advisory committee: £200 to cover the cost of special physical investigations being carried out under the direction of Dr. F. G. Spear at the Strangeways Research Laboratory, Cambridge; £500 for one year to Dr. H. J. Phelps, whilst carrying out experiments in connexion with Dr. Lumsden's anti-cancer serum under the supervision of Dr. Gye and Prof. McIntosh, and £440 for one year to Miss C. F. Fischmann working in the Bernhard Baron institute of pathology at the London Hospital.

Appointments

CRAIG, J. W., M.D. Dub., has been appointed Assistant Medical Officer at Clare Hall Sanatorium (under the Middlesex County Council).

HIGGS, S. L., B.Chir. Camb., F.R.C.S. Eng., Orthopædic Surgeon to St. Bartholomew's Hospital.

JOSEPHS, H., M.R.C.S. Eng., Senior Assistant Medical Officer at the National Sanatorium, Benenden.

MEYER, A., M.B. Cape Town, D.M.R.E., whole-time Officer in the X Ray Diagnostic Department of St. Bartholomew's Hospital.

WEATHERHEAD, E. L., M.B. Lond., Resident Medical Officer at Barking Hospital.

Medical Diary

Information to be included in this column should reach us in proper form on Tuesday, and cannot appear if it reaches us later than the first post on Wednesday morning.

SOCIETIES

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.

TUESDAY, Jan. 19th.

General Meeting of Fellows. 5.30 P.M.

Pathology. 8.30 P.M. (Royal Army Medical College, Millbank, S.W.), W. G. Barnard: 1. Microphotographic Transparencies in Colour. F. J. Sambrook Gowar: 2. Adenoma of the Bronchus. 3. Fibro-adenoma of the Lung. J. Gray: 4. Secondary Carcinoma in the Placenta. A. E. Hamerton: 5. Subacute Combined Degeneration of the Spinal Cord in Captive Monkeys. 6. Meningo-encephalo-myelitis in a Polar Bear. C. C. Holman: 7. Diffuse Polyposis of Intestine. E. J. King and G. A. D. Haslewood: 8. Photometric Measurement with the Ordinary Colorimeter: the Determination of Bilirubin in Blood. A. B. Rosher: 9. An Unusual Agglutinin Response in a Case of Enteric. Dorothy M. Vaux: 10. Two Cases of Congenital morbus cordis in one Family.

THURSDAY.

Dermatology. 4 P.M. (Cases at 5 P.M.) Dr. W. N. Goldsmith: 1. Scleroderma.

Neurology. 8 P.M. Mr. W. Grey Walter: The Electro-encephalogram in Cases of Cerebral Tumour.

FRIDAY.

Disease in Children. 5 P.M. (Cases at 4.30 P.M.) Dr. K. H. Tallerman: 1. Influenzal Meningitis with

Recovery. Dr. Seton Campbell (for Dr. Donald Paterson): 2. Chronic Sinusitis with Early Bronchiectasis. Dr. Charles Kindersley (introduced by Mr. H. C. Edwards): 3. Cirsoid Aneurysm Involving Tongue and Floor of Mouth. Dr. H. J. Wallace: 4. Staphylococcal Pneumonia.

Epidemiology and State Medicine. 8.15 P.M. Mr. B. E. Spear and Mr. A. C. Gould: Mechanical Tabulation of Hospital Records.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, Manson House, 26, Portland-place, W.
THURSDAY, Jan. 21st.—8.15 P.M., Prof. R. P. Strong (Harvard University): Onchocerciasis in Central America and Africa.

HUNTERIAN SOCIETY.
MONDAY, Jan. 18th.—9 P.M. (Mansion House, E.C.), Dr. J. Schoemaker (The Hague): The Surgery of Gastro-duodenal Inflammation.

CHELSEA CLINICAL SOCIETY.
TUESDAY, Jan. 19th.—8.30 P.M. (Hotel Rembrandt, Thurloe-place, S.W.), Dr. Arthur Hurst: Neuromuscular Incoördination of the Gut.

ASSOCIATION OF INDUSTRIAL MEDICAL OFFICERS.
FRIDAY, Jan. 22nd (London School of Hygiene, Keppel-street, W.C.).—4.45 P.M., business meeting. 6 P.M., Prof. Millais Culpin: The Application of Medical Psychology in Industry. Followed by Miss May Smith, D.Sc.
SATURDAY.—10 A.M. (South Metropolitan Gas Co., 589, Old Kent-road, S.E.), Dr. W. D. Jenkins: Clinic and Works Visit.

EUGENICS SOCIETY.
TUESDAY, Jan. 19th.—5.15 P.M. (rooms of the Linnean Society, Burlington House, Piccadilly, W.), Dr. David Forsyth: Heredity versus Environment—a False Issue.

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn-fields, W.C.
MONDAY, Jan. 18th.—5 P.M., Mr. Evelyn Sprawson: Odontomes.
WEDNESDAY.—5 P.M., Dr. Russell Reynolds: Movements of the Œsophagus, Stomach, Duodenum, and Ileum during the Passage of an Opaque Meal.
FRIDAY.—Mr. A. S. Kerr: The Higher Autonomic Control of the Hollow Viscera. (Hunterian lectures.)

UNIVERSITY OF LONDON.
TUESDAY, Jan. 19th.—5 P.M. (University College, Gower-street, W.C.), Prof. J. C. Drummond: Problems of Nutrition. (First of six lectures.)

BRITISH POSTGRADUATE MEDICAL SCHOOL, Ducane-road, W.
MONDAY, Jan. 18th.—2.30 P.M., Dr. H. MacLean: Nephritis and Allied Conditions.
TUESDAY.—2 P.M., pathological demonstration. 3 P.M. Prof. Schoemaker (The Hague): Acute Symptoms in the Upper Abdomen.
WEDNESDAY.—Noon, clinical and pathological conference (medical). 2.30 P.M., clinical and pathological conference (surgical). 4.30 P.M., Mr. A. S. Parkes, F.R.S.: Experimental Endocrinology.
THURSDAY.—Noon, clinical and pathological conference (obstetrics and gynæcology). 2.30 P.M., Dr. Duncan White: Radiological Demonstration. 3.30 P.M., Prof. V. H. Mottram: The Mother's Diet and its Influence on the Fœtus and the Newly Born Child.
FRIDAY.—2 P.M., operative obstetrics. 2.30 P.M., Mr. W. B. Gabriel: Surgical Diseases of the Rectum. 3 P.M., department of gynæcology, pathological demonstration.
Daily, 10 A.M. to 4 P.M., medical clinics, surgical clinics or operations, obstetrical and gynæcological clinics or operations.

WEST LONDON HOSPITAL POST-GRADUATE COLLEGE, Hammersmith, W.
MONDAY, Jan. 18th.—10 A.M., skin clinic. 11 A.M., surgical wards. 2 P.M., operations, surgical and gynæcological wards, medical, surgical, and gynæcological clinics. 4.15 P.M., Mr. Arnold Walker: Genital Prolapse.
TUESDAY.—10 A.M., medical wards. 11 A.M., surgical wards. 2 P.M., operations, medical, surgical, and throat clinics. 4.15 P.M., Mr. Woodd Walker: Pain in the Foot.
WEDNESDAY.—10 A.M., children's ward and clinic. 11 A.M., medical wards. 2 P.M., gynæcological operations, medical, surgical, and eye clinics. 4.15 P.M., Mr. H. P. Gibb: Demonstration of Eye Cases.
THURSDAY.—10 A.M., neurological and gynæcological clinics. Noon, fracture clinic. 2 P.M., operations, medical, surgical, and genito-urinary and eye clinics. 4.15 P.M., Mr. Edgley Curnock: Aspects of Dentistry of Interest to the General Practitioner.
FRIDAY.—10 A.M., medical wards, skin clinic. Noon, lecture on treatment. 2 P.M., operations, medical, surgical, and throat clinics. 4.15 P.M., Dr. H. W. Post: Demonstration of X Ray Films.
SATURDAY.—10 A.M., children's and surgical clinic. 11 A.M., medical wards.
The lectures at 4.15 P.M. are open to all medical practitioners without fee.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, W.
MONDAY, Jan. 18th, to SATURDAY, Jan. 23rd.—ST. JOHN'S HOSPITAL, 5, Lisle-street, W.C., afternoon course in dermatology (open to non-members).—NATIONAL TEMPERANCE HOSPITAL, Hampstead-road, N.W., Tues., 8.30 P.M., Mr. R. Y. Paton: Deformities. Thurs., 8.30 P.M., Mr. C. A. Joll: Thyroid.—NATIONAL HOSPITAL FOR DISEASES OF THE HEART, Westmoreland-street, W., all-day course in cardiology (open to non-members).—ST. PETER'S HOSPITAL, Henrietta-street, W.C., all-day advanced course in urology.—Courses arranged by the fellowship are open only to members.

NATIONAL HOSPITAL, Queen-square, W.C.
MONDAY, Jan. 18th.—3.30 P.M., Mr. Elmquist: Demonstration of Re-educational Methods.
TUESDAY.—3.30 P.M., Dr. Denny-Brown: The Nervous Control of the Sphincters.
WEDNESDAY.—3.30 P.M., Dr. Kinnier Wilson: Clinical Demonstration.
THURSDAY.—3.30 P.M., Dr. Gordon Holmes: Neurosyphilis (I).
FRIDAY.—3.30 P.M., Dr. Walshe: Disseminated Sclerosis (I).
Out-patient clinic daily at 2 P.M.

LONDON SCHOOL OF DERMATOLOGY, 5, Lisle-street, W.C.
TUESDAY, Jan. 19th.—5 P.M., Dr. W. Griffith: Eczema.
WEDNESDAY.—5 P.M., Dr. I. Muende: Histopathology.

HOSPITAL FOR SICK CHILDREN, Great Ormond-street, W.C.
THURSDAY, Jan. 21st.—1 P.M., Dr. Ian Gordon: Modern Therapy in the Anæmias of Childhood. 3 P.M., Mr. A. Simpson-Smith: Bleeding per Rectum.
Out-patient clinics daily at 10 A.M. and ward visits at 2 P.M.

CENTRAL LONDON THROAT, NOSE, AND EAR HOSPITAL, Gray's Inn-road, W.C.
FRIDAY, Jan. 22nd.—4 P.M., Mr. N. Asherson: Pyrexia of Ear, Nose, and Throat Origin.

ST. JOHN CLINIC AND INSTITUTE OF PHYSICAL MEDICINE, 42, Ranelagh-road, S.W.
FRIDAY, Jan. 22nd.—4.30 P.M., Dr. E. P. Poulton: Recent Serological Experiments in the Rheumatic Diseases.

LEEDS GENERAL INFIRMARY.
TUESDAY, Jan. 19th.—3.30 P.M., Mr. Armitage: The Surgical Treatment of Toxic Goitre.

GLASGOW POST-GRADUATE MEDICAL ASSOCIATION.
WEDNESDAY, Jan. 20th.—4.15 P.M. (Royal Infirmary), Mr. Donald Duff: Surgical Cases.

Births, Marriages, and Deaths

BIRTHS

BROWN.—On Jan. 3rd, at Penlea, the wife of Dr. J. Brown, of Bedlington, of a son.
EVERETT.—On Jan. 4th, at Leominster, the wife of Dr. T. F. Everett, of a daughter.
HOLDEN TINCKER.—On Jan. 5th, at Painswick, the wife of Surg. Lt.-Comdr. R. W. Holden Tincker, R.N.V.R., of a daughter.
KIRWAN-TAYLOR.—On Jan. 6th, at Cadogan-square, S.W., the wife of Dr. Gordon Kirwan-Taylor, of a daughter.
LYNAGH.—On Jan. 3rd, at Belfast, the wife of Surg.-Lt.-Comdr. T. B. Lynagh, R.N., of a daughter.
MACLEOD.—On Jan. 3rd, at 27, Welbeck-street, W., the wife of Mr. Cameron MacLeod, F.R.C.S., of a son.
MITCHELL.—On Jan. 4th, at Gipsy Hill, London, S.E., the wife of Dr. T. Carlyle Mitchell, of a son.
WILSON.—On Jan. 7th, at Alexandra Park-road, N., the wife of Dr. G. A. Wilson, Tanganyika Medical Service, of a son.

MARRIAGES

MITCHELL—MCCALLUM.—On Dec. 31st, at Umtali, John C. G. Mitchell, M.B., Rhodesian Medical Service, to Anne, younger daughter of Mr. Colin McCallum, Greenlaw, Berwickshire.
PEENEY—PORTER.—On Jan. 4th, at the Church of the Most Holy Redeemer, Chelsea, Angelo Louis Peter Peeney, M.R.C.S., to Elisabeth Belle Porter, B.Sc., daughter of the late Geoffrey Porter, A.M.I.C.E., of Worthing.
WALLACE—WEATHERHEAD.—On Jan. 2nd, at Chelsea Old Church, Dr. Hugh John Wallace to Dr. Norah Eileen Weatherhead, eldest daughter of the late Canon H. T. C. Weatherhead, of C.M.S., Uganda, and Felstead.

DEATHS

BREEKS.—On Dec. 31st, at Broughton Craggs, Cumberland, Charles Wilkinson Breeks, M.B. Edin., in his 67th year.
RAND.—On Jan. 3rd, at Brightlingsea, Richard Frank Rand, M.D. Edin., F.R.C.S. Eng.
RICHARDSON.—On Jan. 6th, at Brookfield, London, N., William Richardson, M.D. Edin., B.Sc. (Pub. Health), at the age of 80.
SEMPLE.—On Jan. 7th, Lt.-Col. Sir David Semple, M.D., R.U.I., D.Sc. Belf., D.P.H. Camb., R.A.M.C.
SWALLOW.—On Jan. 9th, at East Grinstead, Sussex, Allan James Swallow, M.B. Durh., formerly of Clapham Common, aged 68.
THACKRAH.—On Jan. 10th, at Belsize Park-gardens, Hampstead, N.W., Margaret Grace Thackrah, B.A. Lond., M.D., M.R.C.P. Lond.
THOMPSON.—On Jan. 11th, at Ellerdale-road, Hampstead, N.W., Arthur Hugh Thompson, M.D. Camb., M.R.C.S. Eng., ophthalmic surgeon, aged 77.
TONKS.—On Jan. 8th, at Chelsea, Henry Tonks, F.R.C.S. Eng., formerly Slade Professor of Fine Art in the University of London, aged 74.

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages, and Deaths.

NOTES, COMMENTS, AND ABSTRACTS

THE SUPPLY OF RADIUM

IT seems clear that the trend towards the use of larger radium units will result during the next few years in a demand for radium far beyond the financial resources of the National Radium Trust. This is the conclusion stated in the seventh annual report of the National Radium Trust and Radium Commission 1935–36, which has just been issued (H.M. Stationery Office, Cmd. 5342, 1*s.* 6*d.*). There was a prospect for a time that a further large stock of radium might form part of the national memorial to the late King George, but that prospect has not materialised. In the same report the Commission states that good progress has been made at almost all the national and regional centres. At some of them the volume of work has grown so as to require additional medical personnel and to make it possible to appoint a deputy for the radium officer when on leave or visiting other centres. There is a gratifying tendency to include a physicist in this personnel. Another direction in which growth is desirable is in the provision of pay-beds at centres. Unless these are provided, the middle-class section of the community is largely deprived of the opportunity of radiation treatment, and the Commission is prepared to consider projects by which centres can use national radium for the treatment of patients in pay-beds, up to 20 per cent. of the whole bed provision. The Commission is also advocating a system of outpost centres in the various areas for the purposes of examination, diagnosis, and follow-up. The need for such questing is emphasised by a calculation that, of the 40,000 patients estimated to be suffering from cancer in accessible organs, only about 8000 actually obtain radiation treatment. Delay in seeking assistance, it is suggested, is caused more by fear of the treatment than by ignorance, and there is no doubt that surface radiation does away with many of the objections felt by patients to interstitial radiation. Radium beam treatment is, however, not only costly in time and material but cannot be more widely used without a substantial increase in the amount of radium available, and this consideration is the basis of the Trust's statement that far more radium will shortly be required.

ALCOHOL AND MOTOR ACCIDENTS

AT a meeting of the Society for the Study of Inebriety held on Jan. 12th, Dr. H. M. Vernon pointed out that though road traffic accidents have, in the last two years, receded a little on the maximum observed in 1934, the fatalities still average 18 a day, and the injuries over 600. The Ministry of Transport attributes more of the fatalities to pedestrians than to drivers, but estimates made in other countries assign from 67 to 80 per cent. of them to drivers.

THE SPEED FACTOR

Speed appears to be the most important cause of accidents, and the Ministry of Transport considered that a fourth of the fatalities attributed to drivers in 1935 was due to excessive speed; but many of the other causes tabulated were due in some degree to this cause. The Ministry's data show that private cars and motor cycles incurred their largest proportion of accidents when travelling at a speed of 20 to 40 miles an hour, whilst vans, lorries, and public conveyances incurred their largest proportion at a speed of 10 to 20 miles. As it is estimated that these latter vehicles travel 8 to 16 times further than motor cycles before causing a fatality, and two to three times further than private cars, it appears that there is a close relationship between speed and accidents. In Berlin it was found that when the speed limit for lorries and taxi-cabs was suspended, accidents increased two to threefold; but the rules governing the speed limit of private cars were not altered, and in their case accidents remained unchanged. Converse evidence was obtained in Rhode Island, U.S.A., for when the average speed was reduced from 37 to 31 miles per hour, the fatalities were reduced 27 per cent.

The importance of the speed factor is emphasised because of its relation to the effects of alcohol consumption on drivers. The Committee of the British Medical Association on "The Relation of Alcohol to Road Accidents" reported, in 1935, that very moderate quantities of alcohol (e.g., 3 oz. of whisky) had been shown by psychological tests to diminish attention and control, and to reduce the rapidity and accuracy of coördination with which movements of the eyes, hands, and legs are made. The alcohol must therefore "frequently affect the driving capacity of the driver." It is evident that the adverse effects are more likely to lead to an accident the greater the speed of driving. The influence of a small error becomes magnified in direct proportion to the speed, whilst the distance within which a car can be pulled up when a pedestrian or other possible obstruction is seen varies with the square of the speed. The "reaction time" is increased 0·1 to 0·4 second, and alcohol has the additional effect of causing drivers unconsciously to accelerate their speed. Tests made on twenty subjects by means of a motor driving apparatus showed that after drinking 2·8 oz. of whisky the rate of driving increased 6 per cent. on an average, while the driving errors increased 13 per cent. An acceleration of the kind mentioned indicates the importance of all cars being compulsorily provided with a speedometer.

"UNDER THE INFLUENCE OF——"

The data adduced by the Ministry of Transport indicate that only 1 in 80 of the fatalities attributed to various road users were due to the persons concerned being obviously "under the influence of drink or drugs," but evidence from America suggests that alcohol plays a much larger part in motor accidents. It is stated that though alcohol is directly mentioned in only 7 to 10 per cent. of the fatal traffic accidents, the traffic commissioners believe that probably a third or a fourth of the motor accidents are partly attributable to the consumption of alcohol by the drivers. A new method of obtaining evidence on this problem is now being investigated. It is based on the determination of the alcohol content of small samples of the blood or urine taken from the driver soon after an accident has been incurred.

Estimates made by several independent investigators showed that of the persons having 1·0 part of alcohol per 1000 in their blood, from 40 to 63 per cent. were found to be "under the influence"; of those with 1·7 parts, from 80 to 88 per cent. were so affected, and of those with 2·0 parts, the whole were so affected. As regards the blood analyses made on persons involved in motor and train traffic accidents, two Swedish investigators found that 33 out of the 113 persons tested had more than 1 part of alcohol per 1000 in their blood. An American investigator found that of 119 drivers involved in motor accidents, 11 had 1·4 to 3·5 parts of alcohol in the blood, while 74 of them had more than 0·2 part. Analyses of the blood of 298 persons involved in traffic accidents in Munich showed that only 8 per cent. were practically alcohol-free; 15 per cent. had 0·04 to 1·00 part; 39 per cent. had 1·01 to 2·00 parts, and 37 per cent. had 2·01 parts or more.

The frequency with which large amounts of alcohol were found in the blood in Munich was due to the police having compulsory powers for taking blood samples in cases of accident, and apparently they exercise these powers only when they suspect alcohol as a causative factor. Persons with considerably less than 1 part of alcohol per 1000 in their blood may have their driving adversely affected, even though they do not appear to be "under the influence,"

for it is found that after drinking three ounces of whisky—which produces adverse effects in most persons—the blood is found to contain, as a maximum, 0·3 to 0·4 part of alcohol per 1000.

The logical conclusion is that advanced by the *Times* in a leading article when it said, "As things stand at present there would appear to be no absolute safeguard for the motor driver but total abstinence." Such abstinence should be practiced several hours before driving, as well as during its course, owing to the slowness with which alcohol disappears from the blood.

THE RED CROSS IN SPAIN

A MEMORANDUM from the International Red Cross Committee at Geneva states that 35 national red cross societies have now contributed to the relief of sufferers in the Spanish civil war, their donations amounting to 459,398 Swiss francs, of which over 330,000 francs has come from South America. These gifts are administered by the International Committee with impartiality, and the sums received have made it possible for medical supplies for the treatment of wounded, on both sides, to be sent in increasing quantities. Information bureaux have been established at a number of centres, and delegates of the International Committee are working at Madrid, Valencia, Barcelona, Burgos, Santander, Bilbao, San Sebastian, Alicante, Seville, Saragossa, and Palma de Majorca. The Committee's delegates have been authorised nearly everywhere to visit the prisons, and agreements have been established whereby the release of women, children, boys under 18, adults over 60, and invalids has been secured. Arrangements for the future care of orphans are in train. The delegates have encountered a promising spirit of coöperation on both sides, but a good many difficulties arise in carrying out the letter of the agreements. Unfortunately certain commodities, such as coal, are already scarce in Spain; food rationing is being instituted, and the question whether the Red Cross can undertake the supply of a minimum of the necessities of life to women, children, invalids, and prisoners is under consideration. The sums required would far exceed those received up to the present, and so far the most that can be attempted is the supply of a few parcels of food and condensed milk to sick prisoners.

Donations to the Red Cross Spanish Relief Fund may be sent to the director-general of the British Red Cross Society, 14, Grosvenor-crescent, London, S.W.1.

Messrs. E. MERCK, of Darmstadt, manufacturers of chemicals and medicinal specialties, announce that the selling rights for their preparations in the United Kingdom and Irish Free State are now in the hands of Messrs. Savory and Moore Ltd., of 61, Welbeck-street, London, W.1. Their publicity department, established in this country for the convenience of medical practitioners wanting information and samples of the Merck products, has been moved to 60, Welbeck-street, W.1, and requests should still be directed to this office.

Vacancies

For further information refer to the advertisement columns

Accrington, Victoria Hosp.—H.S., £150.
Arlesey, Beds, Three Counties Hospital.—Temp. Asst. M.O., 7 guineas per week.
Ashton-under-Lyne District Infirmary.—H.S., at rate of £150.
Bath Ear, Nose, and Throat Hospital.—Hon. Asst. Surg.
Beddington and Wallington U.D.C.—M.O.H., £800.
Birmingham City.—Res. Asst. M.O., £400.
Birmingham City, Education Committee.—Part-time Aural Surgeon, 2½ gns. per session.
Birmingham Royal Cripples Hospital.—Res. H.S., at rate of £200.
Blackburn, Brockhall (Certified Institution for Mental Defectives), Langho.—Asst. M.O., £500.
Bootle County Borough.—Asst. M.O.H. and Asst. School M.O., £600.
Calcutta, All India Institute of Hygiene and Public Health.—Director, Rs.1450.
Canterbury, Kent and Canterbury Hosp.—H.P., at rate of £125.
Cardiff Royal Infirmary and Welsh National School of Medicine.—Hon. Dermatologist and M.O. for Male V.D. Centre, at rate of £250.
Carshalton, Queen Mary's Hosp. for Children.—Res. Med. Supt., £1400.
Chesterfield and North Derbyshire Royal Hosp.—H.S. to Ophth. and Ear, Nose, and Throat Depts., at rate of £150.
City of London Hosp. for Diseases of the Heart and Lungs, Victoria Park, E.—H.P., at rate of £100.
Derby, Derbyshire Royal Infirmary.—Gynæcological H.S. and Emergency Anæsthetist, £150.
Dewsbury and District General Infirmary.—Sen. and Second H.S., £200 and £150 respectively.
Doncaster Royal Infirmary and Dispensary.—Res. Surg. O. and Cas. H.S., £250 and £175 respectively.
Ealing Borough.—Res. Asst. M.O., £350.
Eastbourne, Princess Alice Hosp.—Res. H.S., £150.
Eastbourne, Royal Eye Hosp., Pevensey-road.—H.S., £100.
East Ham Memorial Hosp., Shrewsbury-road, E.—H.P., at rate of £150.
Edinburgh, General Board of Control for Scotland.—Deputy Commissioner, £738.
Edinburgh, National Association for the Prevention of Tuberculosis.—Secretary-General in London, £600.
Enfield Urban District Council.—Deputy M.O.H. and Asst. School M.O., £600.
Evelina Hosp. for Sick Children, Southwark, S.E.—H.P., at rate of £120.
Gloucester County Council.—County M.O.H. and School M.O. £1200.
Grimsby and District Hosp.—Surgeon for Orthopædic Dept, and Fracture Clinic, £350. Also Sen. H.S. and H. P., at rate of £200 and £150 respectively.
Halifax Royal Infirmary.—Third H.S., at rate of £150.
Hertford County Hosp.—H.P., at rate of £150.
Hull Municipal Maternity Home and Infants' Hosp.—Jun. Res. M.O., at rate of £100.
Inverness, Royal Northern Infirmary.—Hon. Surgeon to Ear, Nose, and Throat Dept.
Kingston and District Hosp.—Med. Supt., £1200.
Lancaster, Royal Albert Institution for the Feeble Minded.—Res. Jun. Asst. M.O., £375.
Leamington Spa, Warneford General Hospital.—H.P., at rate of £150.
Leeds City.—Part-time M.O. for Transport Dept.
Leeds General Infirmary.—Res. Surg. O., £200.
London County Council.—Asst. M.O.'s, Grade 1, £350.
London Jewish Hosp., Stepney Green, E.—Hon. Surgeon.
Maidstone, West Kent General Hospital.—H.S., £175.
Manchester, Ancoats Hospital.—H.S., at rate of £100. Also Asst. Surg. O., 10s. 6d. per attendance.
Manchester, County Mental Hosp., Prestwich.—Locum Tenens M.O., 5 gns. per week.
Manchester Hospital for Consumption and Diseases of the Throat and Chest.—Asst. M.O. for Crossley Sanatorium, at rate of £200. Also Res. M.O. for St. Anne's Home, £200.
Manchester, Northern Hospital, Cheetham Hill-road.—Res. H.P. and Res. H.S., each at rate of £100.
Manchester, Withington Hospital.—Cons. Obstet. and Gynæcologist, at rate of £300.
Metropolitan Hosp., E.—Psychiatrist.
Middlesex Hosp., W.—Res. M.O., £400.
Newcastle-upon-Tyne Hosp. for Sick Children.—Sen. Res. M.O., £250. Also H.P. and H.S., each at rate of £100.
Newcastle-on-Tyne, Wooley Sanatorium, near Hexham.—Asst. M.O., £350.
Newport, Mon., Royal Gwent Hosp.—Sen. H.S. Also second H.S., at rate of £250 and £135 respectively.
Peppard Common, Oxon, Berks and Bucks Joint Sanatorium.—H.P., £250.
Preston, Sharoe Green Hosp.—Jun. Asst. Res. M.O., at rate of £100.
Princess Elizabeth of York Hosp. for Children, Shadwell, E.—Asst. Surg.
Rhondda Urban District Council.—Asst. M.O., £500.
Romford, Oldchurch Hosp.—Jun. Res. M.O., £250.
Royal London Ophthalmic Hosp., City-road, E.C.—Gifford Edmonds Prize in Ophthalmology, £100. Also Hon. Asst. Physician.
St. Albans County Institution, Oster House.—H.S., at rate of £150.
Shrewsbury, Royal Salop Infirmary.—Res. H.S., at rate of £160.
Southend-on-Sea General Hosp.—First H.S., at rate of £100.
Stoke-on-Trent, Burslem, Haywood, and Tunstall War Memorial Hosp.—Res. H.S., at rate of £175.
Stoke-on-Trent, Stanfield Sanatorium.—Res. M.O., £350.
Surrey County Council.—Asst. M.O., £600.
Torquay, Torbay Hosp.—Locum Tenens Res. H.P., 6 gns. a week.
University College Hosp., Gower-street, W.C.—Registrar to X Ray Therapy Dept., £250.
Victoria Hospital for Children, Tite-street, Chelsea, S.W.—Cas. O., at rate of £200. Also H.P. and H.S., each at rate of £100.
West End Hospital for Nervous Diseases, 73, Welbeck-street, W.—Hon. Psychotherapist. Also two Res. H.P.'s, each £125.
Wolverhampton Royal Hosp.—Asst. Res. M.O. to Gynæcological and Obstet. Dept., at rate of £100.
Medical Referee under the Workmen's Compensation Act, 1925, for the Deal, Dover, Folkestone, and Hythe County Court Districts (Circuit No. 49). Applications should be addressed, the Private Secretary, Home Office, Whitehall, London, S.W.1, before Feb. 3rd.